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ULTRAVIOLET RADIATIONS

MEASUREMENT BY THE ACETONE METHYLENE BLUE METHOD *

C. H. BEST, M.D.

AND

J. H. RIDOUT, M.A.

TORONTO

A great variety of methods has been suggested for the assay of solar radiations of wave lengths less than 320 millimicrons. Webster, Hill and Eidinow [1] have used the rate of bleaching of a standard acetone methylene blue solution exposed in a quartz tube. The bleaching [2] of this solution has been standardized against the lethal dose for *Infusoria* under certain standard conditions and against the erythema-producing dose for the skin of the average white arm. These authors state that each unit of the methylene blue scale equals from 2 to 4 erythema doses.[2] It is stated elsewhere [3] that two lethal doses for *Infusoria* are sufficient to produce a mild erythema. The exact limits of the spectrum between which the acetone methylene blue is reduced are not accurately known. Webster, Eidinow and Hill [2] state that the solution absorbs all rays shorter than 360 millimicrons. Russell and Massengale [4] believe that the reagent is sensitive only to wave lengths shorter than 320 millimicrons. The solution, as supplied by Siebe Gorman, is certainly appreciably faded by wave lengths that penetrate ordinary window glass. The temperature coefficient of the bleaching of acetone methylene blue by ultraviolet radiations has not, to our knowledge, been adequately investigated. Webster, Hill and Eidinow [1] state that a rise in temperature of 10 C. makes the reading of 0.6 too high. It is true that the erythema-producing action of ultraviolet radiations is increased by a rise in temperature, but it is not probable that the curve of increase would be the same as that of the acceleration of bleaching of the acetone

* Received for publication, Sept. 9, 1927.

* Read at the Thirty-Ninth Annual Meeting of the American Pediatric Society, Chesapeake Bay, May, 1927.

* From the Section of Physiological Hygiene, School of Hygiene, University of Toronto.

1. Webster, A.; Hill, L., and Eidinow, A.: Lancet **1**:745, 1924.
2. Hill, Leonard: Nature **115**:642, 1925.
3. Eidinow, A.: Brit. J. Tuberc. **19**:113, 1925.
4. Russell, W. C., and Massengale, O. N.: Science **65**:619, 1927.

methylene blue solution. Furthermore, recent work [5] makes it probable that the therapeutic effect of ultraviolet radiations is not proportional to the erythema produced. For these reasons, the fading of the acetone methylene blue should be studied at a constant temperature. The readings given in the table were not taken at a constant temperature, but the conditions under which they were observed are comparable to those which existed in other localities from which values have been reported. In the future, arrangements for the maintenance of a constant temperature will be necessary. The effect of temperature and other physical factors should also be accurately controlled in animal experiments, since dilated capillaries in the skin may render available a much larger proportion of ultraviolet radiations than constricted ones.

Ultraviolet Radiations as Measured by Acetone Methylene Blue Method

1927, Week Ending	Acetone Methylene Blue Units per Week	Average for Each Day	1927, Week Ending	Acetone Methylene Blue Units per Week	Average for Each Day
January 8....	14.0	1.85	April 9.....	22.5	....
January 15...	16.0	....	April 16.....	34.5	3.88
January 22...	11.0	....	April 23.....	31.0	....
January 29...	14.5	....	April 30.....	25.5	....
February 5...	8.0	....	May 7.....	26.0	....
February 12..	9.5	1.51	May 14.....	31.0	....
February 19..	9.0	....	May 21.....	43.0	....
February 26..	11.0	....	May 28.....	53.0	5.8
March 5.....	17.0	....	June 4.....	48.0	....
March 12.....	14.5	....	June 11.....	49.5	....
March 19.....	13.5	2.22	June 18.....	64.5	....
March 26.....	14.0	....	June 25.....	70.5	9
April 2.....	17.0	....	June 30.....	69.5	....

The standard quartz tube containing the acetone methylene blue solution was exposed in a vertical position at the end of a long pole erected on the roof of a four story building.

The readings given in the table were taken over a portion of the same period that was studied by Tisdall and Brown.[5] It was hoped that the acetone methylene blue method could thus be correlated with the formation of bone in rats fed on a rachitic diet. A certain degree of correspondence between the results obtained by the two methods is seen to exist. In view of the variable effect of temperature on the solution and possibly also on the rats, and the fact that the acetone methylene blue method measures wave lengths longer than the therapeutic range, a closer relationship could not be expected.

5. Tisdall, F. F., and Brown, Alan: Am. J. Dis. Child., this issue.

SEASONAL VARIATION OF THE ANTIRACHITIC EFFECT OF SUNSHINE*

FREDERICK F. TISDALL, M.D. (TOR.)
AND
ALAN BROWN, M.B. (TOR.)
TORONTO

A study of the literature on the etiology of rickets shows that practically no progress was made in the elucidation of the cause of this condition from the time of Glisson [1] until the investigations of the past ten years. The theories advanced were almost without number [2] and were apparently limited only by the imagination of the different investigators. Credit belongs to Mellanby,[3] in 1918, for directing attention to the presence and importance of an antirachitic factor, or vitamin, in the prevention of this disease. Whether this factor was identical with or just allied to vitamin A was not clear until McCollum, Simmonds, Becker and Shipley,[4] in 1922, produced conclusive evidence of the presence of a separate and distinct antirachitic vitamin which has since been designated as vitamin D. The most concentrated source of this vitamin is cod liver oil.

The curative action of ultraviolet rays from a mercury vapor quartz lamp on rachitic patients exposed to these rays was first demonstrated by Huldschinsky,[5] in 1919. His observations were soon confirmed by numerous investigators. Hess and Unger,[6] in 1921, first demonstrated the curative effect of sunshine in cases of infantile rickets. Their observations were corroborated by experiments on animals by Powers,

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* From the Laboratories of the Sub-Department of Pediatrics, University of Toronto, and the Hospital for Sick Children.

* Read at the Fifth Annual Meeting of the Canadian Society for the Study of Diseases of Children, Toronto, June 13 and 14, 1927.

1. Glisson, F.: De rachitide, London, 1650.
2. Tisdall, F. F.: Canad. M. A. J. **11**:934, 1921.
3. Mellanby, E.: J. Physiol. **52**:11, 1918.
4. McCollum, E. V.; Simmonds, M.; Becker, J. E., and Shipley, P. G.: J. Biol. Chem. **53**:292, 1922.
5. Huldschinsky, K.: Deutsche med. Wchnschr. **45**:712, 1919.
6. Hess, A. F., and Unger, L. J.: Cure of Infantile Rickets by Sunlight. J. A. M. A. **77**:39 (July 2) 1921.

Park, Shipley, McCollum and Simmonds,[7] and by Hess, Unger and Pappenheimer.[8] The next great step in the knowledge of the etiology of rickets was a discovery made independently by three groups of investigators: Rosenheim and Webster [9] in England and Hess, Weinstock and Helman,[10] and Steenbock and Black [11] in the United States. These workers showed that inert food containing cholesterol or allied substances could be made antirachitic by exposure to ultraviolet rays. This important discovery has been further investigated, and during the past few months, after a number of suggestive investigations,[12] with the cooperation of Professor Windaus of Germany,[13] Hess in the United States [14] and Rosenheim and Webster [15] in England, it has been shown that cholesterol is not the activated substance, but that it is ergosterol which is usually present in cholesterol as an impurity in the proportion of 1 to 2,000 parts. An indication of the potency of this substance is shown by the fact that the daily administration of 0.0001 mg. of activated ergosterol to a rat that is being fed on a rachitogenic diet cures or prevents the disease, and that 5 mg. of this substance produces the same antirachitic effect as 1 liter of active cod liver oil.

The antirachitic effect of the rays from a mercury vapor quartz lamp and from the sun is due to certain rays in the ultraviolet portion of the spectrum. As the present report is concerned entirely with the effect of the sun's rays, the spectrum of the sun will be considered with some detail. The most exhaustive studies of sunshine in relation to health

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7. Powers, G. F.; Park, E. A.; Shipley, P. G.; McCollum, E. V., and Simmonds, N.: Prevention of the Development of Rickets in Rats by Sunlight, J. A. M. A. **78**:159 (April) 1922.

8. Hess, A. F.; Unger, L. F., and Pappenheimer, A. W.: J. Biol. Chem. **50**:77, 1922.

9. Rosenheim, O., and Webster, T. A.: Lancet **1**:1025 (May 16) 1925.

10. Hess, A. F.; Weinstock, M., and Helman, F. D.: J. Biol. Chem. **63**:305 (March) 1925.

11. Steenbock, H., and Black, A.: J. Biol. Chem. **64**:263 (June) 1925.

12. Hess, A. F., and Weinstock, M.: J. Biol. Chem. **64**:193, 1925. Hess, A. F., and Windaus, A.: Proc. Soc. Exper. Biol. & Med. **24**:171, 1926; **24**:369, 1927. Schultz, F. W., and Morse, M.: Spectroscopic Observations on Cod Liver Oil, Am. J. Dis. Child. **30**:199 (Aug.) 1925. Schlutz, F. W.; Ziegler, M. R., and Morse, M.: J. Biol. Chem. **73**:209, 1927. Rosenheim, O., and Webster, T. A.: Biochem. J. **21**:127, 1927.

13. Isolation of Vitamins, Berlin Letter, J. A. M. A. **88**:854 (March 12) 1927.

14. Hess, A. F., and Windaus, A.: Proc. Soc. Exper. Biol. & Med. **24**:461, 1927.

15. Rosenheim, O., and Webster, T. A.: Biochem. J. **21**:389, 1927.

have been made by Dorno.[16] Sunshine is composed of invisible heat rays which have wave lengths longer than 760 millimicrons (a millimicron is one millionth of a millimeter in length), visible light which varies in length from 760 to 380 millimicrons and invisible ultraviolet rays which range from 380 to 290 millimicrons. The heat rays constitute about 60 per cent of the solar radiations, the visible rays 40 per cent and the ultraviolet rays less than 1 per cent.[17] Hess and Weinstock,[18] in 1923, showed that the ultraviolet rays effective in the cure and prevention of rickets "must have a wave length not longer than 302 or possibly 313 millimicrons." In 1927, the same investigators,[19] as the result of irradiating cholesterol, concluded that "the 302 line possessed marked antirachitic potency whereas the 313 line exerted very slight specific power." It is thus evident that the effective rays in sunshine for the prevention and cure of rickets are the shortest ultraviolet rays present, and that they range in length from 290 to 313 millimicrons.

A study of the factors influencing the amount of these rays that reach us is of the greatest importance. Pettit [20] has shown that the amount of ultraviolet rays radiated from the sun varies with the number of the sun spots, but it is beyond the scope of this paper and our knowledge to discuss this aspect of the problem intelligently. It is probable that these variations, although of importance, are slight as compared with the variations produced by the absorption of these rays by the earth's atmosphere under different conditions.

The short ultraviolet rays are readily cut off by the smoke, dust and moisture in the atmosphere. It is, therefore, evident that they will be markedly reduced in the winter and in the early morning and late afternoon, when the rays of the sun pass through a greater distance of atmosphere than when the sun is high in the sky. In the Swiss Alps at Davos, Dorno [17] found that the ultraviolet content of the midday sun in January was only about 10 per cent as great as that of the midday sun in July. He also found that the shortest ultraviolet rays found at midday in December were 12 millimicrons longer than those found in July. With the exception of the determination just reported by Best

16. Dorno, C.: Klimatologie im Dienste der Medizin, Brunswick, Vieweg & Son, 1920; General Remarks on Meteorology and Climatology, Brunswick, Vieweg & Son, 1924.

17. Dorno, (footnote 16, first reference).

18. Hess, A. F., and Weinstock, M.: Study of Light Waves in Their Relation to Rickets, J. A. M. A. **80**:687 (March 10) 1923.

19. Hess, A. F., and Weinstock, M.: Proc. Soc. Exper. Biol. & Med. **24**:759, 1927.

20. Pettit, E.: Publications of the Astronomical Society of the Pacific, **38**:21 (Feb.) 1926.

and Ridout,[21] measurements of these rays in Canada or in the United States have not been recorded.

The investigations of Dorno in the Alps were made with cadmium photoelectric cells, which are slightly sensitive to ultraviolet rays as long as 366 millimicrons. As this extends far past the antirachitic range, it cannot be assumed that the antirachitic effect of sunshine will vary exactly with his measurements. Although they are of the greatest value and interest, they cannot be applied without reservations to the conditions found in the southern part of Canada and the northern part of the United States, on account of local weather conditions and the difference in altitude.

The seasonal variation in the incidence of rickets is one of the striking features of the disease. It was commented on at length by Kassowitz [22] as long ago as 1884. In view of the present knowledge of the rôle played by sunshine in the prevention and cure of this disease through irradiation of both food and people, the importance of a study of the seasonal variation of its antirachitic effect is at once apparent.

EXPERIMENTAL WORK

Many difficulties were encountered in planning an experiment of this type to extend over a period of one year. We chose the albino rat as our experimental animal, and the question at once arose as to how this animal would stand the exposure to a temperature below zero during the winter; information concerning this could not be found in the literature. Rather than hazard the risk of having the rats perish in winter, we constructed a specially heated cage (fig. 1). This consisted of an ordinary circular cage which is placed on top of a zinc drum. In the center of the floor of the cage, a circular opening was cut and covered with wire mesh. The drum with the cage attached to it was placed over the heating element which consisted of from one to five ordinary large carbon filament incandescent lamps. The hot air rises through the opening in the floor of the cage, and the rats sit over this opening or not, as they desire. The whole heating element was built inside a tub (fig. 2). This acts as a windbreak but does not interfere with the exposure of the rats to sunshine. No casualties resulted from cold even on the days when the temperature dropped to 15 F. below zero. The rats did so well that if we were planning the experiment again, we would be tempted to omit the heat, as the electric installation for our numerous units on the roof of the laboratory was a considerable item (fig. 3).

The longest daily duration of exposure was arbitrarily set at two hours. An examination of the records furnished by the Dominion Meteorological Bureau, situated within half a mile of the hospital, showed the impossibility of attempting to obtain throughout the year a daily exposure to sunshine for two hours. From the practical standpoint, it would be more valuable to put the rats out for two hours daily, just as an infant would be placed outdoors, regardless of the amount of sunshine during this period. Consequently, an exposure for two

21. Best, C. H., and Ridout, J. H.: Am. J. Dis. Child., this issue, p. 719.
22. Kassowitz, M.: Wien. med. Presse **38**:97, 1897.

Fig. 1.—Specially constructed cage to supply the rats with heat through the central opening in the floor of the cage.

Fig. 2.—Heating element built inside a tub. The cage is placed over this heating element, and the tub acts as a windbreak.

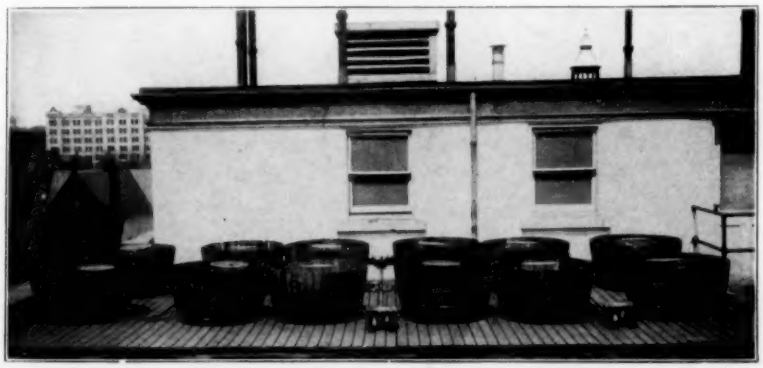

Fig. 3.—Tubs installed on the roof of the laboratory south of the animal room.

hours means that sunshine was available for a certain percentage of this time, while for the remainder of the time the rats received skylight or reflected light from the clouds and sky. Naturally, less sunshine was secured during the winter than during the summer, but this does not interfere with the practical value of the conclusions.

The time of day for exposure was from 11 a. m. to 1 p. m., or certain fractions of this period. The place of exposure was on the roof of the laboratory south of the animal room. This is five stories above the level of the street and almost in the geographic center of the city. The manufacturing and business sections are situated to the south, however, and with the prevailing west winds, the atmosphere was reasonably clear of smoke. Control rats were kept in the animal room. Special precautions were taken to prevent the entrance of ultraviolet rays. The windows were made opaque, and a screen was placed in front of the door to prevent any direct light falling on the animals when the door was opened. The degree of darkness inside is indicated by the fact that electric lights were necessary for ordinary lighting purposes. Although little light entered from the outside, adequate ventilation was provided.

The rats, which were all albinos, were obtained from a local source under conditions controlled by us. The food of the breeding rats was kept unchanged throughout the period of the experiment. When milk was used, it was evaporated milk, and an excess of vitamin D was not allowed in the diet, since it was shown by Korenchevsky and Carr[23] as early as 1923, that the protective substances can be transferred to the young with the mother's milk. Direct light was not allowed to enter the breeding room, as it has been shown by Steenbock, Hart, Hoppert and Black,[24] in the goat, and by Hess, Weinstock and Sherman,[25] in man, that irradiation of the lactating parent increases the antirachitic property of the milk secreted. The importance of this whole problem of the care and food of the breeding rat has been carefully studied by Smith and Chick,[26] who state: "Very young animals possess reserve stores of these factors (vitamins A and D) to a surprisingly variable degree, depending on the diet of the mother before and during pregnancy and during the period of lactation."

The methods employed to determine the degree of rickets were: (1) estimation of the inorganic phosphorus in the blood; (2) determination of the percentage of ash in the bones and (3) roentgen-ray examination of the long bones of the legs.

It was first shown, in 1920, by Iversen and Lenstrup[27] and by Howland and Kramer,[28] that the concentration of the inorganic phosphorus in the blood of rachitic infants is markedly reduced. These investigators also showed that the

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23. Korenchevsky, V., and Carr, M.: J. Path. & Bact. **26**:389, 1923.

24. Steenbock, H.; Hart, E. B.; Hoppert, C. A., and Black, A.: J. Biol. Chem. **66**:441, 1925.

25. Hess, A. F.; Weinstock, M., and Sherman, E.: Antirachitic Properties Developed in Human Milk by Irradiating Mother, J. A. M. A. **88**:24 (Jan. 1) 1927.

26. Smith, H. H., and Chick, H.: Biochem. J. **20**:131, 1926.

27. Iversen, P., and Lenstrup, E., cited by Howland and Kramer: Calcium and Phosphorus in Serum in Relation to Rickets, Am. J. Dis. Child. **22**:105 (Aug.) 1921.

28. Howland and Kramer (footnote *27*).

administration of cod liver oil produced a decided increase in the inorganic phosphorus coincident with the cure of the patient. It was then demonstrated independently by Hess and Unger,[29] Howland, Kramer and Casparis[30] and one of us[31] (F. F. T.) that the cure of patients who had rickets by exposure to ultraviolet rays is accompanied by the same definite increase in the inorganic phosphorus in the blood as already noted after the administration of cod liver oil. This observation has been confirmed repeatedly by many investigators who have used different types of animals, including the rat.[32] Recently, Koch and Cahan[33] reported that direct irradiation of young rats fed on McCollum's rachitogenic diet 3143[34] had little if any influence on the inorganic phosphorus in the blood, although the development of rickets was prevented. We cannot suggest an explanation of these results, as a survey of our figures obtained from several hundred rats showed a direct relation between the amount of irradiation and the concentration of the inorganic phosphorus in the blood.

We determined the amount of inorganic phosphorus in the whole blood rather than in the serum. It would have been preferable to use serum, but we did not do so because it was difficult to obtain sufficient material. The method that one of us[35] (F. F. T.) devised for serum was applied to 1 cc. of whole blood, with satisfactory results. Fiske and Subbarow[36] have shown that there is no danger of incomplete extraction of inorganic phosphorus from whole blood by the addition of a solution of trichloracetic acid.

As early as 1842, Marchand[37] showed that the bones of a rachitic child contain less calcium and more organic material than the bones of a nonrachitic infant. Bethke, Steenbock and Nelson, in 1923,[38] emphasized the necessity of previous extraction of the variable lipoidal and fat content of the bones with alcohol and ether before the percentage of ash is determined. The value of this method of determining the degree of rickets has been clearly demonstrated by Dutcher and his confreres.[39] In England, Chick, Korenchevsky and Roscoe[40] state: "If chemical examination is used in the diagnosis of rickets, the best criterion of defective calcification is given by the value of the ratio of the amount of ash to the amount of organic material contained in fat extracted bone."

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29. Hess, A. F., and Unger, L. J.: Use of Carbon Arc Light in Prevention and Cure of Richets, J. A. M. A. **78**:1596 (May 27) 1922.

30. Howland, J.; Kramer, B., and Casparis, H.: Ultraviolet Radiation in Rickets, Am. J. Dis. Child. **24**:20 (July) 1922.

31. Tisdall, F. F.: Canad. M. A. J. **12**:536, 1922.

32. Kramer, B., and Howland, J.: Bull. Johns Hopkins Hosp. **33**:313, 1922.

33. Koch, E. M., and Cahan, M. H.: Proc. Soc. Exper. Biol. & Med. **24**:153, 1926.

34. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **47**:507, 1921.

35. Tisdall, F. F.: J. Biol. Chem. **50**:329, 1922.

36. Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**:375, 1925.

37. Marchand, R. F.: J. f. prakt. Chem. **27**:83, 1842.

38. Bethke, R. M.; Steenbock, H., and Nelson, M. T.: J. Biol. Chem. **58**:71, 1923.

39. Dutcher, R. A.; Creighton, M., and Rothrock, H. A.: J. Biol. Chem. **66**:401, 1925; Dutcher, R. A., and Kruger, J. H.: J. Biol. Chem. **69**:277, 1926.

40. Chick, H.; Korenchevsky, V., and Roscoe, M. H.: Biochem. J. **20**:622, 1926.

We determined the percentage of ash in the bones by the method outlined by Bethke, Steenbock and Nelson.[35] The femora and tibiae of from two to five rats were dissected from the adhering soft tissue and were dried at from 90 to 95 C. for two days. Any remaining soft tissue was scraped off. The bones were then ground in a mortar, transferred to an extraction thimble, allowed to stand in 95 per cent alcohol for twenty-four hours and then extracted with ether in a Soxhlet apparatus for twenty-four hours. After the extraction, the residue of bone was dried at from 90 to 95 C. for one hour, carefully weighed and then incinerated in an electric muffle furnace. In the early part of the experiment, the incineration was done with a gas burner by the Stolte method.[41] After cooling it in a desiccator, the material was again weighed and the percentage of ash calculated in the bone from which the fat had been extracted.

From twenty-five to forty rats were started every Monday, beginning in October, 1926. They were from 25 to 27 days of age and weighed about 40 Gm. The age and condition of the rat at the beginning of the experiment is of prime importance. Some of the rats were given a normal diet and used as controls. Sunshine apparently did not produce any effect on these rats. The majority of the rats were placed on McCollum's rachitogenic diet 3143 (wheat 33 per cent, corn 33 per cent, wheat gluten 15 per cent, gelatin 15 per cent, sodium chloride 1 per cent, and calcium chloride 3 per cent). A few of these were kept in the darkened room, while the others were placed outside at midday daily, including Sundays. The duration of daily exposure was varied from five minutes to two hours.

The average increase in percentage in weight over a period of four weeks under different conditions was as follows: rachitogenic diet, inside, 67.1; rachitogenic diet, outside, in sun two hours daily, 77.1; normal diet, 165.4.

At first, some rats were killed from each cage at the end of each week. It was found, however, that it required four weeks to produce the desired degree of rickets in the control animals that were fed on the rachitogenic diet. As no advantage was gained by prolonging this period, the rats were killed at the end of four weeks by being bled from the carotid artery while under light ether anesthesia. The blood was collected in oxalated tubes (10 mg. potassium oxalate per five cubic centimeters), and the inorganic phosphorus was estimated. Roentgenograms were then taken, and the ash content of the bone was determined.

Each week two new rats, just received (aged about 25 to 27 days), were killed, and the amount of inorganic phosphorus in the blood and the percentage of ash in the bone were determined. The inorganic phosphorus usually varied from 7 to 7.5 mg. per hundred cubic centimeters of whole blood and the ash from 38 to 42 per cent.

EFFECTS OF EXPOSURE TO SUNSHINE

The typical results obtained with rats placed on the normal diet and rats kept inside on the rachitogenic diet are shown in table 1. The inorganic phosphorus in the blood of the normal rat decreases only slightly in four weeks, while the blood of the rachitic rat shows a tremendous decrease. The results on the ash in the bone are just as striking. The percentage of ash in the bones of the normal rat increases from 40 to almost 60, while in the rachitic rat it decreases to slightly over 30. The evidence of rickets was just as marked in the rats killed in May and June as in those killed in the winter.

41. Stolte, K.: Biochem. J. **35**:104, 1911.

The antirachitic effect of a daily exposure to sunshine from 11 a. m. to 1 p. m. over a period of four weeks, throughout the month of December, 1926, and January, February, March, April and May, 1927, is shown in table 2. In order to give a more graphic presentation of these results, they are plotted in figures 6 and 7. Figures 8 and 9 show the result of the experiment on rats placed on a rachitogenic diet.

TABLE 1.—*The Inorganic Phosphorus in the Blood and the Percentage of Ash in the Bones of Rats Kept Indoors and Fed on Rachitogenic Diet and on Normal Diet*

	Rachitogenic Diet		Normal Diet	
	Inorganic Phosphorus per 100 Cc. of Blood Mg.	Percentage of Ash in Bone	Inorganic Phosphorus per 100 Cc. of Blood Mg.	Percentage of Ash in Bone
At beginning of experiment Age of rats from 25 to 27 days	7.5	40.0	7.5	40.0
2 weeks later	2.8	39.0	7.3	46.3
3 weeks later	2.2	....	7.2	55.8
4 weeks later	1.6	32.0	6.3	59.4

TABLE 2.—*Antirachitic Effect on Rats of Two Hours' Daily Exposure to Sunshine for Four Weeks During the Period from 11 a. m. to 4 p. m.*

	Rachitogenic Diet				Normal Diet			
	Inorganic Phosphorus per 100 Cc. of Blood Mg.		Percentage of Ash in Bone		Inorganic Phosphorus per 100 Cc. of Blood Mg.		Percentage of Ash in Bone	
Rats Killed	Rats Kept Indoors	Rats Kept Outside	Inside Rats	Outside Rats	Inside Rats	Outside Rats	Inside Rats	Outside Rats
1926								
Nov. 28	1.6	2.7	....	....	6.1	7.2	....	....
Dec. 5	2.0	2.6	....	....	...	...	....	....
Dec. 12	...	...	....	....	7.4	7.7	....	....
Dec. 19	2.0	2.2	35.0	....	5.7	5.5	59.5	61.4
Dec. 26	1.5	2.6	27.4	27.8	7.0	...	56.7	....
1927								
Jan. 3	1.2	2.9	30.3	43.7	...	6.5	....	56.7
Jan. 10	1.6	3.5	35.4	33.7	6.8	7.3	55.8	58.1
Jan. 17	...	3.1	38.4	43.9	...	...	....	....
Jan. 24	2.2	3.0	38.4	38.4	...	...	....	....
Jan. 31	2.4	3.4	39.2	44.0	...	...	....	....
Feb. 7	1.8	2.6	26.7	37.5	...	7.7	....	57.4
Feb. 14	1.6	2.4	32.4	36.7	6.8	8.5	57.1	57.7
Feb. 21	...	3.2	....	39.9	...	...	....	....
Feb. 28	1.4	4.5	32.0	51.0	...	...	....	....
March 7	2.0	4.9	39.6	43.6	...	6.3	....	55.9
March 14	1.9	4.5	34.6	51.0	6.3	...	59.4	....
March 21	...	...	....	....	...	...	....	....
March 28	1.2	5.2	33.4	50.4	...	...	....	....
April 4	1.7	5.7	31.2	51.9	...	...	....	....
April 11	...	...	....	46.7	6.7	...	58.4	58.4
April 18	1.6	5.1	33.8	54.4	...	...	....	....
April 25	1.4	4.0	34.8	50.5	...	...	....	....
May 2	2.1	4.5	34.7	44.3	...	...	....	....
May 9	...	4.6	28.0	48.1	6.0	...	....	....
May 16	...	...	....	....	...	...	....	....
May 23	1.3	4.8	28.1	47.1	...	...	....	....

Fig. 4.—Roentgenogram of a rat fed on a rachitogenic diet for four weeks. The rat was kept inside and was killed on Dec. 27, 1926.

Fig. 5.—Roentgenogram of a rat fed on a normal diet; killed Jan. 3, 1927.

The results recorded show that in Toronto there is a slight but definite antirachitic effect of sunshine during the winter. This has already been recorded.[42] At the end of February and during the first week in March, a sharp increase occurs, which is maintained throughout April and May.

The antirachitic effect of different periods of daily exposure to sunshine throughout the four weeks ending May 9 are given in table 3.

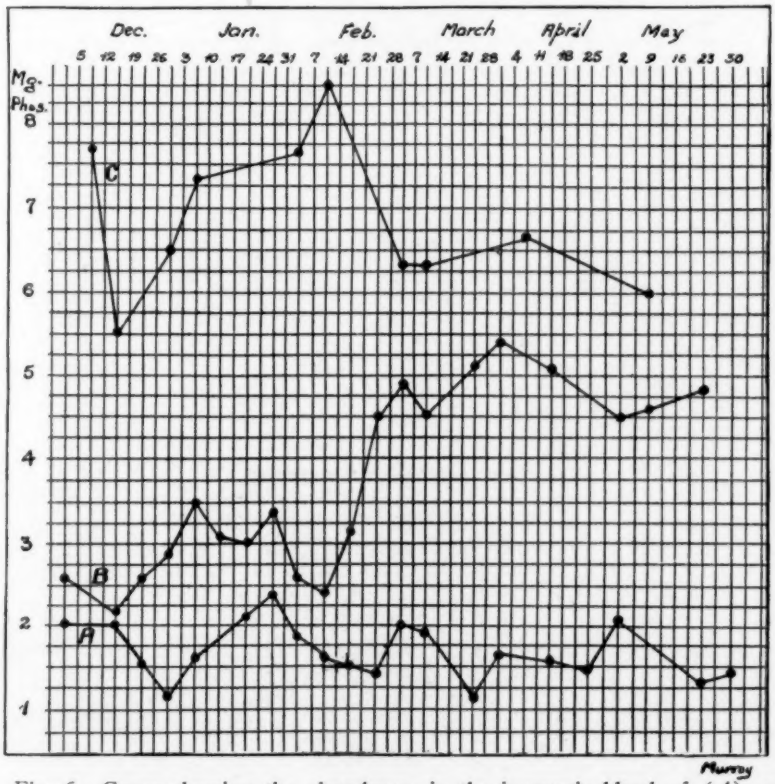

Fig. 6.—Curve showing the phosphorus in the inorganic blood of (*A*) rats fed on a rachitogenic diet for four weeks without exposure to the sunshine. *B* indicates the curve of rats fed on rachitogenic diet for four weeks with a daily exposure to the sunshine for two hours and *C* the curve of control rats fed on a normal diet.

From these figures it is evident that the antirachitic effect of the sunshine in April and May, during the hours of 11 a. m. and 1 p. m., is approximately eight times as great as during December, January and the greater part of February.

42. Tisdall, F. F., and Brown, Alan: Proc. Soc. Exper. Biol. & Med. **24**:446, 1927.

TABLE 3.—*Antirachitic Effect of Different Daily Periods of Exposure to Sunshine Throughout Four Weeks Ending May 9, 1927*

Rats	Inorganic Phosphorus per 100 Cc. of Blood Mg.	Percentage of Ash in Bone
Exposed ¼ hour daily.....	2.6	41.2
Exposed ½ hour daily.....	3.4	44.9
Exposed 1 hour daily.....	4.2	47.5
Exposed 2 hours daily.....	4.6	48.1

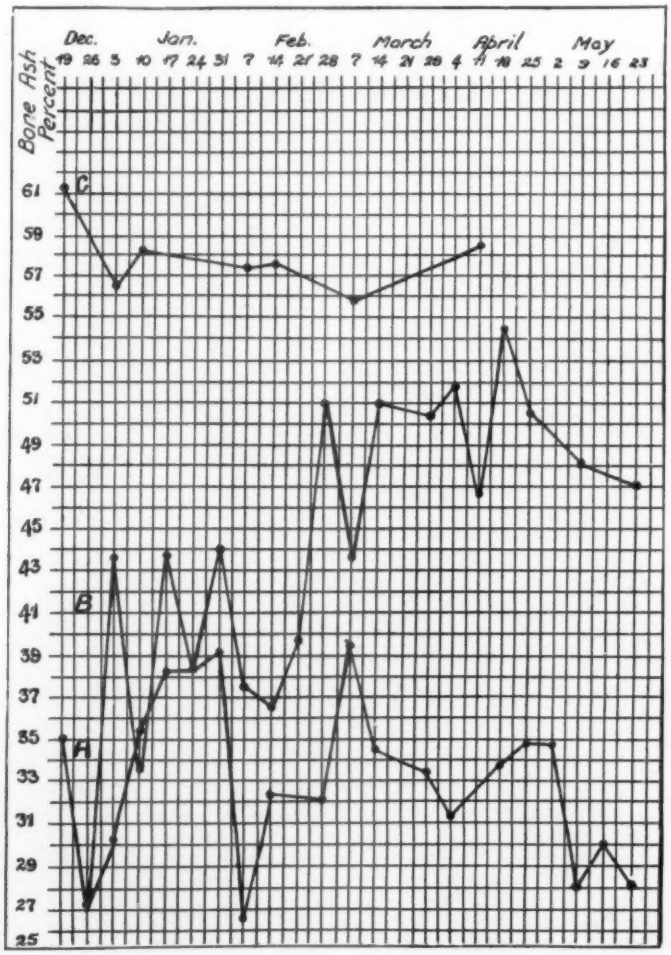

Fig. 7.—Curve showing the percentage of ash in the bones of (*A*) rats fed on a rachitogenic diet for four weeks without exposure to the sunshine. *B* indicates the curve of rats fed on a rachitogenic diet for four weeks with daily exposure to the sunshine for two hours and *C*, the curve of control rats fed on a normal diet.

Fig. 8.—Roentgenogram of a rat fed on a rachitogenic diet for four weeks with daily exposure to the sunshine for two hours; killed, Dec. 20, 1926.

Fig. 9.—Roentgenogram of a rat fed on a rachitogenic diet for four weeks with daily exposure to the sunshine for two hours; killed, May 23, 1927.

Fresh cold air as an antirachitic factor was studied and found to have absolutely no effect. The possibility that the shavings of wood used as bedding might become antirachitic was considered, as it has been shown by Rosenheim and Webster [43] that sterols extracted from wood shavings can be rendered antirachitic by exposure to ultraviolet rays. Rats were kept in cages which were placed in the sun two hours daily, the rats being kept inside during this period; no antirachitic effect was observed.

Our results in regard to the seasonal variation of the antirachitic effect of sunshine are of greater value for areas in approximately the same latitude as Toronto, as the antirachitic effect of sunshine is deter-

TABLE 4.—*The Average Number of Hours of Sunshine Each Day for Three Years Recorded by the Month*

	Hours per Day		Hours per Day
January	2.0	July	9.5
February	3.5	August	8.4
March	4.9	September	5.2
April	7.1	October	5.0
May	7.4	November	3.0
June	9.2	December	1.9

TABLE 5.—*Average Percentage of Maximum Sunshine from 11 a. m. to 1 p. m. for Three Years and for 1927, Recorded by the Month*

	Average for Three Years	1927		Average for Three Years	1927
	Percentage	Percentage		Percentage	Percentage
January	30	41	July	76	..
Febuary	40	33	August	71	..
March	45	51	September	56	..
April	67	64	October	53	..
May	68	48	November	43	..
June	70	..	December	26	..

mined to a large degree by the height of the sun in the sky, which in turn varies with the latitude. The map of the North American continent shows that Toronto is in the same latitude as many of the thickly populated northern states, a fact which is seldom realized.

The averages of the hours of sunshine daily for each month during three years are given in table 4. The averages of the percentage of maximum sunshine from 11 a. m. to 1 p. m. for each month for three years are given in table 5; the average daily percentage of maximum sunshine from 11 a. m. to 1 p. m. for December, 1926, to May, 1927, is given in the same table.

These results for the midday period are not only of interest in view of the daily exposure of the rats for two hours, but are also of

43. Rosenheim, O., and Webster, T. A.: Biochem. J. **20**:1340, 1926.

more value than the total daily hours of sunshine for comparative purposes, since infants cannot be exposed to the available sunshine from sunrise to sunset. Considering the average values, it is seen that from 11 a. m. to 1 p. m. in January, the sun was shining less than one third of the time; in April it shone two thirds of the time, while in July it had increased to three fourths of the time.

The average daily hours of sunshine a week from 11 a. m. to 1 p. m. is given in table 6. The antirachitic effect of sunshine, as determined biologically on rats, increased tremendously during the last week in February and the first week in March (table 2). A study of tables 2 and 6 indicates that there is apparently little relationship between the amount of available sunshine and the increase in its antirachitic effect.

TABLE 6.—*Average Daily Hours of Sunshine Per Week During the Period Between 11 a. m. to 1 p. m.*

1926 Week Ending	Average Hours Per Day	1927 Week Ending	Average Hours Per Day
December 4	0.68	March 5	1.30
December 11	0.57	March 12	1.15
December 18	0.68	March 19	0.51
December 25	0.02	March 26	0.85
1927		April 2	1.27
January 1	0.64	April 9	1.41
January 8	0.75	April 16	1.42
January 15	1.41	April 23	1.04
January 22	0.51	April 30	1.40
January 29	0.71	May 7	1.14
February 5	0.54	May 14	0.51
February 12	1.05	May 21	1.14
February 19	0.28	May 28	1.13
February 26	0.50		

Also, the results reported by Best [21] do not indicate a marked increase in ultraviolet radiation at this time, as compared with January.

The most probable explanation of the sudden increase of the antirachitic effect of the sun's rays in March is that there is an increase in the shorter and more effective rays. According to Dorno,[17] the shortest rays in March, as measured in Switzerland, were 306 millimicrons, while in April they were as short as 299 millimicrons. The importance of this is at once evident in view of the work of Hess and Weinstock,[18] who showed that rays 313 millimicrons in length had little antirachitic effect, while rays 302 millimicrons in length were extremely effective.[44]

A study of the effect of sunshine on the resistance to infection of rats that are fed on a rachitogenic diet has been made by E. Chant

44. After the present paper was written, there appeared a most interesting article on ultraviolet radiation from sunlight by Bundesen, Lemon, Falk and Coade (J. A. M. A. **89**::187 [July 16] 1927), in which it was recorded that the shortest ultraviolet rays in Chicago sunshine at the beginning of February were 303 millimicrons in length, while at the beginning of March the shortest were 301 millimicrons.

Robertson in the Connaught Laboratories, University of Toronto, and is being reported elsewhere.[45]

This investigation of the seasonal variation of the antirachitic effect of sunshine is being continued throughout the summer and autumn.

CONCLUSIONS

1. The sun's rays during December, January and February in the latitude of Toronto produce a slight but definite antirachitic effect on rats fed on a rachitogenic diet.

2. A sharp increase occurs in the antirachitic effect of sunshine about the first of March.

3. The antirachitic effect of sunshine in April and May is approximately eight times as great as in December, January and February.

4. It would appear that the increase in the antirachitic effect of sunshine in March, April and May is due not so much to an increase in the amount of the ultraviolet rays of the length present in the sunshine in winter as to the presence of rays that are shorter than those found during the winter.

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45. Robertson, E. C.: Canad. M. A. J. **17**:1033 (Sept.) 1927.

ANTIRACHITIC EFFECT OF SKYSHINE*

FREDERICK F. TISDALL, M.D. (TOR.)
AND
ALAN BROWN, M.B. (TOR.)
TORONTO

The term "skyshine" is used to designate the sun's rays that are reflected from the sky and clouds in contradistinction to the rays received directly from the sun itself. An object placed on the sunny side of a street receives not only rays from the sun, but also the reflected rays from the sky. If an object is placed on the shady side of the street, only the rays reflected from the sky (skyshine) are received. If the object is again placed on the sunny side of the street and if a long cylinder pointed directly at the sun is placed over the object, the rays from the sky are cut off by the walls of the cylinder, and only the rays directly from the sun pass along the inside of the cylinder to the object at the bottom.

No studies on the antirachitic effect of skyshine have been recorded. In 1920, Dorno [1] reported that when the sun is at its height in the sky, the reflected ultraviolet rays from the sky (skyshine) are 15 per cent greater in amount than the ultraviolet rays received from the sun directly. In order to remove any confusion concerning the exact meaning of this statement, we may say that, according to Dorno, if an object is placed on the shady side of the street with the sun at its height, the object will receive 15 per cent more ultraviolet radiation than if it is placed at the bottom of a cylinder which cuts off the skyshine and allows only the direct rays from the sun to fall on it. In 1925, Leonard Hill [2] confirmed Dorno's observation. Marvin, chief of the Weather Bureau, United States Department of Agriculture, Washington, in discussing a paper by Kimball [3] on "Records of Total Solar Radiation Intensity and their Relation to Daylight Intensity," said [4]: "While this paper does not deal with ultraviolet radiation, the indications from the color-temperature

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* From the Laboratories of the Sub-Department of Pediatrics, University of Toronto, and the Hospital for Sick Children.
* Read at the Thirty-ninth Annual Meeting of the American Pediatric Society, Chesapeake Bay, May, 1927.

1. Dorno, C.: Klimatologie im Dienste der Medizin, Brunswick Vieweg & Son, 1920.
2. Hill, L.: Nature **115**:642, 1925.
3. Kimball, H. H.: Monthly Weather Review **52**:473, 1924.
4. Marvin, C. F.: Personal communication.

of skyshine and the data of tables 1 and 2 lead to the conclusion that skyshine as compared to direct sunshine must be relatively rich in ultraviolet radiation." As any antirachitic effect of direct or reflected solar radiation is due to the short ultraviolet rays,[5] these observations are of considerable interest.

In the preceding paper,[6] we have described the procedure employed for the determination of the antirachitic effect of sunshine. The rats used were placed on the laboratory roof on the sunny side of the animal room for definite periods each day. At the end of four weeks, they were killed and examined. Strictly speaking, the animals received not

TABLE 1.—*The Antirachitic Effect of Skyshine on Rats*

	Rachitic Diet Inorganic Phosphorus, per 100 Cc. of Blood			Rachitic Diet Percentage of Ash in Bone			Normal Diet Sunlight 11-1 Daily	
Period, Four Weeks Ending	Inside Cage Mg.	Skyshine 11-1 Daily Mg.	Sunshine 11-1 Daily Mg.	Inside Cage	Skyshine 11-1 Daily	Sunshine 11-1 Daily	Inorganic Phosphorus per 100 Cc. of Blood Mg.	Percentage of Ash in Bone
Jan. 3, 1927....	1.2	2.4	2.9	30.3	40.5	43.7	6.5	56.7
Feb. 28, 1927...	1.4	2.7	4.5	32.0	44.6	51.0	6.3	55.9
March 28, 1927..	1.2	2.7	5.2	33.4	46.2	50.4	...	....
April 11, 1927..	...	3.6	7.2	....	51.3	46.7	6.7	58.4
April 18, 1927..	1.6	...	5.1	33.8	....	54.4	...	....
April 25, 1927..	1.4	4.0	...	34.8	50.0	....	...	....

TABLE 2.—*Measurements of the Ultraviolet Content of Available Sunshine, Including Reflected Light From the Sky and Skyshine Alone (Hill's Methylene Blue Solution)*

Date	Skyshine Units	Sunshine Units	Skyshine / Sunshine Per Cent
April 25, 1927.....	1.5	2.5	60
April 27, 1927.....	2.0	3.0	66
April 28, 1927.....	3.0	5.0	60
April 29, 1927.....	2.0	4.0	50
May 2, 1927.....	2.0	4.0	50

only sunshine but skyshine as well. The conditions, however, are comparable to those obtained when an infant is placed outdoors in the sun.

In order to study the antirachitic effect of skyshine, we placed similar rats on the laboratory roof on the north or shady side of the animal room, as shown in figure 1. It is seen that the conditions are not even as favorable as would be obtained when an infant is placed outdoors on the shady side of the street, as some of the skyshine was cut off, not only by the wall of the animal room, but by wooden ventilators on each

5. Hess, A. F., and Weinstock, M.: A Study of Light Waves in their Relation to Rickets, J. A. M. A. **80**:687 (March 10) 1923.

6. Tisdall, F. F., and Brown, A.: Am. J. Dis. Child., this issue, p. 721.

side. The rats, four or five in each cage, were fed McCollum's rachitogenic diet 3143 [7] and placed outdoors daily from 11 a. m. to 1 p. m. for four weeks. They were then killed. The inorganic phosphorus in the blood was determined, roentgenograms taken, and the percentage of ash in the bones determined.[6] The blood from all the rats in one cage and the bones were pooled before examination in order to minimize the effect of any individual variations. The results are given in table 1. Roentgenograms of the bones of the rats killed in January are shown in figures 2, 3 and 4. Figure 2 is that of a rat kept inside; figure 3, a rat exposed to skyshine two hours daily, and figure 4, a rat exposed to sunshine two hours daily.[8]

Fig. 1.—Rats exposed to skyshine on the north, or shady side of the animal room.

In table 2 are given measurements of the ultraviolet content of the available sunshine, which includes the reflected rays from the sky and the ultraviolet content of skyshine alone. The latter measurements were made on the shady side of a building throughout the day. These measurements were obtained by Hill's methylene blue method [9] and furnished to us by Prof. C. H. Best, of the department of physiological hygiene, University of Toronto.

7. McCollum, E. V.; Simmonds, H.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **47**:507, 1921.

8. Dr. A. H. Rolph of the X-ray Department of the Hospital for Sick Children supplied the roentgenograms.

9. Best, C. H., and Ridout, J. H.: Am. J. Dis. Child., this issue, p. 719.

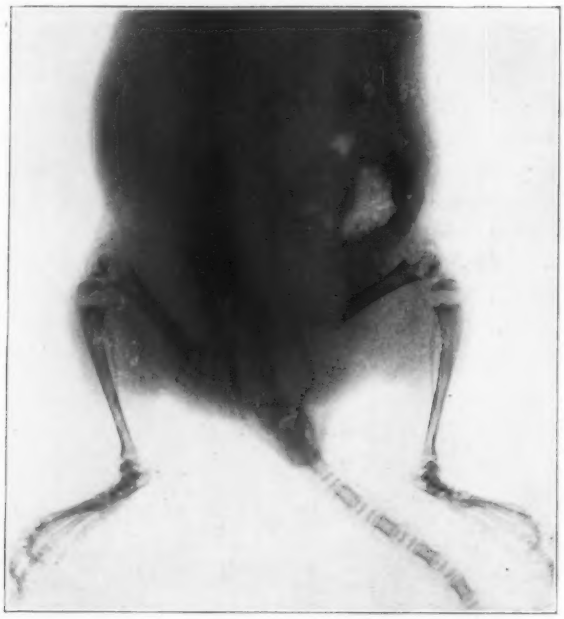

Fig. 2.—Roentgenogram of rat on rachitogenic diet for four weeks with no exposure; killed, Jan. 3, 1927.

Fig. 3.—Roentgenogram of rat on rachitogenic diet for four weeks, exposed to skyshine two hours daily; killed, Jan. 3, 1927.

From a study of the roentgenograms and of tables 1 and 2, it would appear that the antirachitic effect of skyshine is approximately from one-half to two-thirds as great as that produced by what is ordinarily termed sunshine (rays from the sun plus reflected rays from the sky).

In view of the antirachitic effect of skyshine, which does not cause "sunburn," it is of interest to note that the burning or reddening of the skin, which is usually taken as the unit of measurement of ultraviolet therapy, must now be regarded as an accompanying phenomenon which may or may not be a measurement of the amount of ultraviolet rays received.

Fig. 4.—Roentgenogram of rat on rachitogenic diet for four weeks, exposed to sunshine two hours daily; killed, Jan. 3, 1927.

CONCLUSIONS

1. The antirachitic effect of skyshine (reflected rays from the sky and clouds) is approximately from one-half to two-thirds as great as that produced by what is ordinarily termed sunshine (rays from the sun plus the reflected rays from the sky).

2. Reddening of the skin by ultraviolet rays is not a suitable unit for measurement of ultraviolet therapy. It should be considered simply as an accompanying phenomenon which may or may not be a measurement of ultraviolet rays received.

ANTIRACHITIC VALUE OF THE SUN'S RAYS THROUGH VARIOUS SPECIAL WINDOW GLASSES*

FREDERICK F. TISDALL, M.D. (TOR.)
AND
ALAN BROWN, M.B. (TOR.)
TORONTO

At least three special glasses are on the market at present, which, according to the claims of the manufacturers, will transmit the antirachitic rays of sunshine. These glasses are: (1) Vitaglass—manufactured in England and marketed in the United States by the Vitaglass Corporation, New York; (2) Vioray glass—marketed in Canada by W. E. Phillips Company, Oshawa, Ontario, and (3) Corning special glass—manufactured by the Corning Glass Works, Corning, N. Y. Vioray and Corning glass have been available for only a short time.

In February, 1927, we reported that "Rays from December sunlight which had passed through Vitaglass had an antirachitic effect which was roughly one-fourth the value of the direct rays. Rays which had passed through ordinary glass had no antirachitic effect."[1] Subsequently, in a report on window substitutes approved by the Council on Physical Therapy of the American Medical Association,[2] it was shown that the sun's rays through Vitaglass produced an antirachitic effect on rachitic chickens. In the same report, it was also shown by spectroscopic measurements that both Vitaglass and Corning glass transmitted rays of known antirachitic value (shorter than 313 millimicrons in length). Similar spectroscopic studies with Vitaglass have been recorded by Sheard[3] and by Bundesen and others.[4]

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* This work was aided by a grant from the Department of Health of the Province of Ontario.

* From the Laboratories of the Sub-Department of Paediatrics, University of Toronto, and the Hospital for Sick Children.

1. Tisdall, F. F., and Brown, A.: Proc. Soc. Exper. Biol. & Med **24**:449, 1927.

2. Report on Window Glass Substitutes, J. A. M. A. **88**:1562 (May 14) 1927.

3. Sheard, C.: Ultraviolet Radiations and Its Transmission by Various Substances, J. A. M. A. **88**:1315 (April 23) 1927.

4. Bundesen, H. N.; Lemon, H. B.; Falk, I. S., and Coade, E. N.: Ultraviolet Radiation from Sunlight and Incandescent Lamps: Its Transmission Through Window Glass, J. A. M. A. **89**:187 (July 19) 1927.

In the course of our studies on the antirachitic effect of sunshine, throughout the year, we investigated the antirachitic value of the sun's rays through Vitaglass, Vioray glass and Corning glass. Our experiments were started with Vitaglass last fall.[5] Investigations were begun on Vioray glass and Corning glass as soon as we could obtain them. The general method of procedure has been described in a preceding paper.[6]

Rats were placed on McCollum's rachitogenic diet 3143.[7] Control rats were kept inside, while the others were placed outside, in cages on the laboratory roof, from 11 a. m. until noon or 1 p. m., daily. These cages were covered by a special enclosure made of the glass to be investigated, as illustrated in figure 1. Further

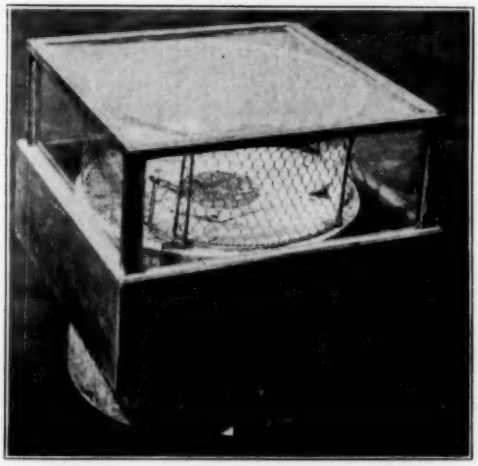

Fig. 1.—Special glass enclosure over rat cage exposed on the laboratory roof.

control rats fed on a normal diet were also used. After a period of four weeks, all the rats were killed; the antirachitic effect was then measured by roentgenograms of the hind legs[8] and in estimations of the inorganic phosphorus of the blood and of the percentage of ash in the bones. The results are shown in table 1 and in figures 2 to 8.

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5. A personal communication from the Vitaglass Corporation received in August, 1927, states that, according to transmission tests by the Bureau of Standards, the transmission of ultraviolet rays by Vitaglass has been improved since the glass used by us was manufactured.

6. Tisdall, F. F., and Brown, A.: Seasonal Variation of the Antirachitic Effect of Sunshine, Am. J. Dis. Child., this issue, p. 721.

7. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: J. Biol. Chem. **47**:507, 1921.

8. Dr. A. H. Rolph, in charge of the X-Ray Department of the Hospital for Sick Children, supplied the roentgenograms.

The antirachitic effect of December, January and February sunshine through Vitaglass, as measured by the inorganic phosphorus in the blood and by the percentage of ash in the bones, is just as unfavorable as that obtained with ordinary window glass. Figures 2 to 5, however, demonstrate that, whereas there is no evidence of any antirachitic effect of the rays through ordinary glass, there is a slight but definite antirachitic effect of the rays through Vitaglass at this time of the year. About March 1, owing to the great increase in the therapeutic value

Fig. 2.—Roentgenogram of rat on rachitogenic diet for four weeks; no exposure; killed Dec. 27, 1926.

of the sun's rays,[6] the antirachitic effect of the rays through Vitaglass is marked. As shown in table 1 and in figures 6, 7 and 8, similar results were obtained with Vioray and Corning glass.

It is to be noted that obvious differences cannot be detected in the efficacy of the three special glasses. Through the aid of Prof. C. H. Best, measurements were made by the methylene blue method [9] of the relative amounts of ultraviolet radiation entering the different cages.

9. Best, C. H., and Ridout, J. H.: The Measurement of Ultraviolet Radiations, Am. J. Dis. Child., this issue, p. 719.

TABLE 1.—*The Antirachitic Effect of Sunshine Through Special Glasses*

Exposure for Four Weeks Ending 1926	Daily Length of Exposure Hours	Ordinary Window Glass: Inorganic Blood Phosphorus per 100 Cc. Mg.	Ordinary Window Glass: Percentage of Ash in Bones	Vitaglass: Inorganic Blood Phosphorus per 100 Cc. Mg.	Vitaglass: Percentage of Ash in Bones	Vioray Glass: Inorganic Blood Phosphorus per 100 Cc. Mg.	Vioray Glass: Percentage of Ash in Bones	Corning Glass: Inorganic Blood Phosphorus per 100 Cc. Mg.	Corning Glass: Percentage of Ash in Bones
Dec. 20...	2	1.6	28.5	1.6	31.2	...	....	...	....
1927	.	...	....	...	....	..	....	...	....
Jan. 17...	2	2.2	32.0	2.4	34.8	...	....	...	....
Feb. 21..	2	2.6	40.0	2.4	28.0	...	....	...	....
March 28.	2	2.5	34.1	...	49.3	...	....	...	....
April 25..	2	2.4	42.3	4.3	47.9	...	....	...	....
June 20..	1	2.4	33.3	3.6	41.3	3.4	43.7	3.1	....
July 18...	1	...	....	...	....	3.5	36.9	...	....
Aug. 8...	1	1.6	37.4	2.4	38.4	...	....	...	41.0

TABLE 2.—*Measurements of the Ultraviolet Content of Sunshine Through Various Special Glasses (Leonard Hill's Methylene Blue Solution)*

Date 1927	Ordinary Glass, Units	Vioray Glass, Units	Vitaglass, Units	Corning Special Glass, Units
May 30.....	1.0	2.5	2.0	2.0
May 31.....	3.0	6.5	6.0	5.5
June 3.....	2.5	6.5	5.5	5.5
June 6.....	3.5	6.5	4.5	5.5
June 8.....	3.5	5.0	7.0	6.5
June 9.....	3.0	5.5	6.0	3.5
Average	2.7	5.4	5.1	4.7

TABLE 3.—*The Antirachitic Effect of Daily Exposure to Direct Sunshine for Varying Periods*

Exposed for 4 Weeks Ending	Inorganic Blood Phosphorus, Mg. per 100 Cc. Blood: No Exposure	15 Minute Exposure Daily	30 Minute Exposure Daily	1 Hour Exposure Daily	2 Hour Exposure Daily	Percentage of Ash in Bones: No Exposure	15 Minute Exposure Daily	30 Minute Exposure Daily	1 Hour Exposure Daily	2 Hour Exposure Daily
May 9....	...	2.6	3.4	4.2	4.6	28.1	41.2	44.9	47.5	48.1
May 23....	1.3	...	...	3.9	4.8	28.1	....	....	48.7	47.1
June 6....	...	3.3	...	4.5	4.3	....	41.3	43.9	47.8	46.3
June 20...	1.6	...	3.6	...	...	24.9	....	40.1	....	....
June 27...	2.2	3.3	...	4.1	4.8	38.0	43.0	....	43.1	48.5
Aug. 1....	1.4	...	3.1	...	...	26.8	....	43.5	....	....
Average.	1.6	3.0	3.3	4.1	4.6	29.2	41.8	43.1	46.7	47.5

The measurements, which are only comparative, are given in table 2. The results with the Corning glass are slightly less favorable than those with the other special glasses, but this is probably explained by the fact that the sample of Corning glass was thick and unpolished.

The antirachitic effect of different daily lengths of exposure to direct sunshine during May, June and July is given in table 3. A comparison of these results with those obtained by a one hour daily exposure to sunshine through the special glasses (table 1) leads to the

Figure 3

Figure 4

Fig. 3.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed two hours daily, under ordinary glass; killed Dec. 20, 1926.

Fig. 4.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed two hours, daily, under Vitaglass; killed Dec. 20, 1926.

conclusion that the antirachitic effect of the sun's rays through Vitaglass, Vioray and Corning glass is from 25 to 50 per cent of the antirachitic effect obtained without the use of glass.

From the results in tables 1 and 3, it would appear that the sun's rays through ordinary glass may produce a just perceptible antirachitic

effect. The roentgenograms, however, do not show evidence of any antirachitic effect. It may be concluded, therefore, that there is either no antirachitic effect of the sun's rays through ordinary window glass, or, at most, a negligible effect. This is in accord with previous observations.[10]

We attempted to determine the antirachitic value of rays through an ordinary sized window glazed with Vioray glass under conditions similar to those found in the average home.

Fig. 5.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed two hours, daily, without glass; killed Dec. 20, 1926.

Rats were placed in cages situated 1, 3 and 5 feet from a standard sized window. The glass in the lower sash measured 25 by 30 inches (63 by 76 cm.). The glass in the upper sash was of the same size. The window faced directly east. The rats were exposed daily from 8 a. m. until 12 noon, for a period of four weeks. Direct sunshine, however, did not fall on the rats during the whole of the daily period of exposure. The cage 1 foot (30 cm.) from the window was

10. Hess, A. F., and Weinstock, M.: Study of Light Waves in their Relation to Rickets, J. A. M. A. **80**:687 (March 10) 1923.

Figure 6

Figure 7

Fig. 6.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed one hour, daily, under Vitaglass; killed June 20, 1927.

Fig. 7.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed one hour, daily, under Vioray glass; killed June 20, 1927.

Fig. 8.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed one hour, daily, under Corning special glass; killed June 20, 1927.

entirely in the sunshine until 8:35. At that time, owing to the change of the sun's position in the sky, one corner of the cage did not receive the direct rays, and by 10:15 no direct rays fell on the cage. The cage 3 feet (91 cm.) from the window was entirely in the sunshine until 8:15. By 8:45 no direct rays from the sun fell on this cage. The cage 5 feet (152 cm.) from the window did not receive direct sunshine at any time. All cages, of course, received skyshine throughout the period of exposure.[11]

We similarly exposed rats in cases placed 1, 3 and 5 feet (30, 91 and 152 cm.) from an open window in the next room. The window had the eastern exposure already noted. The lower sash was completely raised, as with any ordinary window. A blind covered the upper, unopened, part. Thus the rays entered from an area one half the size of the Vioray window. In addition, this open area was covered with an ordinary wire fly screen. After four weeks, on August 1, the rats were killed and examined.

TABLE 4.—*The Antirachitic Effect of the Sun's Rays Through an Ordinary Sized Window Glazed with Special Glass (Vioray) and Through an Open Window*

	Lower Open Window; Eastern Exposure		Lower Open Window; Southern Exposure		Upper and Lower Windows Glazed with Vioray Glass; Eastern Exposure	
Cages Situated from Window	Inorganic Blood Phosphorus per 100 Cc. Mg.	Percentage of Ash in Bones	Inorganic Blood Phosphorus per 100 Cc. Mg.	Percentage of Ash in Bones	Inorganic Blood Phosphorus per 100 Cc. Mg.	Percentage of Ash in Bones
1 foot.....	3.3	41.7	2.8	36.6	3.4	43.0
3 feet.....	2.9	37.1	2.4	....	2.5	39.0
5 feet.....	2.5	30.6	1.5	25.9	2.3	31.4

In order to determine whether there was any difference between an eastern exposure and a southern exposure, we placed cages 1, 3 and 5 feet (30, 91 and 152 cm.) from an open window of the same size with a southern exposure. This open area was also covered with an ordinary wire fly screen. However, owing to the position of the sun in the sky, only about one fourth of the cage 1 foot (30 cm.) from the window received direct sunshine, and then only for one and one-half hours daily, from 10:30 until 12 o'clock. The rats in this cage always remained in the back of the cage, so in reality they received only skyshine. Direct sunshine did not fall on the other two cages. Thus, in this experiment, we really measured the antirachitic effect of skyshine coming through an open window with a southern exposure.

The results of these experiments, recorded in table 4 and figures 9, 10 and 11,[12] indicate that an exposure for four hours, from 8 a. m. until 12 noon, 1 foot (30 cm.) from an open window covered with wire fly

11. Tisdall, F. F., and Brown, A.: The Antirachitic Effect of Skyshine, Am. J. Dis. Child, this issue, p. 737.

12. The roentgenograms of the rats exposed in front of the open windows are essentially the same as the roentgenogram in figures 9, 10 and 11.

screen, and with an eastern exposure, or 1 foot (30 cm.) from a window twice the size, glazed with Vioray glass, is approximately equal in its antirachitic effect to a thirty minute exposure outside in the sun at noon hour. It would also appear that the antirachitic effect of the skyshine entering under the foregoing conditions, with either an eastern or a southern exposure, is slight—in fact, almost negligible—except

Figure 9

Figure 10

Fig. 9.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed from 8 a. m. to 12 noon, daily, in a cage situated in a room, 1 foot (30 cm.) from an ordinary sized window glazed with Vioray glass; eastern exposure; killed Aug. 1, 1927.

Fig. 10.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed from 8 a. m. to 12 noon, daily, in a cage situated in a room, 3 feet (91 cm.) from an ordinary sized window glazed with Vioray glass; eastern exposure; killed Aug. 1, 1927.

immediately adjacent to the window. Thus, to obtain much benefit from rays coming through an open window or through a window glazed with special glass, it is necessary to receive the direct rays of the sun.

In order to obtain a useful percentage of the antirachitic effect of skyshine approximately equal to that of the direct rays of the sun,[11]

it would be necessary to construct a solarium of special glass, as it is obvious that the percentage of available skyshine that can enter through the area of a window, as situated in an ordinary room, is small.

CONCLUSIONS

1. The antirachitic effect of the sun's rays (including skyshine) through Vitaglass, Vioray glass and Corning special glass is from

Fig. 11.—Roentgenogram of rat on rachitogenic diet for four weeks; exposed from 8 a. m. to 12 noon, daily, in a cage situated in a room, 5 feet (152 cm.) from an ordinary sized window glazed with Vioray glass; eastern exposure; killed Aug. 1, 1927.

25 to 50 per cent of the antirachitic effect obtained without the use of glass.

2. Obvious differences could not be detected in the efficacy of the three glasses.

3. No antirachitic effect, or at the most a negligible effect, is produced by the sun's rays through ordinary glass.

4. The antirachitic effect of skyshine through an ordinary window glazed with special glass (Vioray) is slight—in fact, almost negligible—

except immediately adjacent to the window. Similar results were obtained with rays through an open window covered with ordinary fly screen.

5. In order to obtain much benefit from rays through an open window, or a window glazed with special glass, it is necessary to receive the direct rays of the sun.

6. The use of special glass during the winter months is probably of little value. Its use in the latitude of Toronto is justified from about the first of March on, as the inclement spring weather prohibits the exposure of patients to the sun's rays, which at that time have a great antirachitic effect.

DOES THE IRRADIATION OF COD LIVER OIL INCREASE ITS ANTIRACHITIC POTENCY?*

EDWIN T. WYMAN, M.D.
ARTHUR D. HOLMES, PH.D.
LAWRENCE W. SMITH, M.D.
DONALD C. STOCKBARGER, Sc.D.
AND
MADELEINE G. PIGOTT, B.S.
BOSTON

The results obtained in a previously reported study [1] of the effect of irradiation of cod liver oil showed that the antirachitic value of the oil is not enhanced by irradiation with ultraviolet rays from a quartz mercury lamp. In the preliminary study, the irradiated cod liver oil was fed to experimental animals for a period of ten days in amounts not exceeding 3 mg. Since it was felt that the amount of irradiated oil fed, or the length of the experimental period, or both, may have been insufficient, a second study has been made in which 15 mg. of an irradiated cod liver oil was fed to the experimental animals for a period of six weeks. A comment on this study, together with the results obtained, forms the basis of the present communication.

NATURE OF OIL

The oil used in the earlier test was not available for the present study. Accordingly, a fresh supply of oil, typical of high grade medicinal cod liver oil, was procured for the experiments reported here. It was manufactured from fresh livers by the open kettle steam process at plants located in Massachusetts, Maine and Nova Scotia. Crude oils from these sources in the ratio of 26 per cent, 9 per cent and 65 per cent,

TABLE 1.—*Chemical and Physical Characteristics*

Specific Gravity	Refraction Index	Saponification Value	Iodine Number	Free Fatty Acid, per Cent
0.919	1.476	188.74	147.52	0.654

respectively, were thoroughly blended and cold pressed to remove the cod liver stearin. The chemical and physical characteristics of the pressed oil, as determined by the usual analytic methods, are shown in table 1.

* Received for publication, June 20, 1927.

* From the Infants' and Children's Hospital, Boston; the Pediatric and Pathological Departments, Harvard Medical School and the Research Laboratory of the E. L. Patch Co.

1. Wyman, E. T.; Holmes, A. D.; Smith, L. W.; Stockbarger, D. C., and Piggott, M. G.: Boston M. & S. J. **195**:525 (Sept. 9) 1926.

The vitamin A content of the oil was determined by the method given in the United States Pharmacopoeia [2] and was found to be 1,200 vitamin A units per gram.

IRRADIATION OF OIL

As pointed out in the earlier paper,[1] before irradiation of the cod liver oil was attempted, a study was made to ascertain the depth that ultraviolet rays penetrate cod liver oil. It was found that a layer of cod liver oil a few hundredths of a millimeter thick absorbs ultraviolet rays of less than 0.26 microns in length, and that cod liver oil 1 mm. deep is opaque to ultraviolet rays of all wave lengths. In view of the slight depth to which ultraviolet rays penetrate cod liver oil, it was decided to adopt carefully controlled conditions for stirring the oil during irradiation. In this instance, a supply of cod liver oil was divided into three lots; one lot was reserved in its natural condition, one was irradiated for one-half hour, and the third was irradiated for two hours with a 3 inch horizontal direct current Cooper Hewitt Uviarc, which had previously been used about 250 hours. The lamp was operated at 4.2 amperes and 83 volts across the arc.

One hundred cubic centimeters of cod liver oil was irradiated at a time in an 8 inch, flat bottomed, crystallizing dish. The oil was maintained at a constant temperature of 25 C. during the period of irradiation by placing the crystallizing dish in a circulating water bath at a constant level. The depth of the oil was just sufficient to submerge a glass stirring rod 4 mm. in diameter. In order that a fresh surface of oil should be constantly exposed to the action of the ultraviolet radiation, the oil was continually stirred with an inverted T-shaped stirring rod. The combined lengths of the blades of the stirring rod practically equaled the diameter of the crystallizing dish. To prevent a shadow being cast on the oil by the mechanism of stirring, the lamp was placed a little to one side of the axis of the dish. The distance of the lamp from the plane of the oil was 11 inches (28 cm.), while the distance from the center of the oil surface was 12 inches (30 cm.). The stirring rod was driven by a small electric motor at a uniform rate of 100 revolutions a minute, a speed just under that which would cause whipping and consequent spattering of the oil. We adopted this method of constantly bringing the fresh surface of oil in contact with the ultraviolet radiation in order that in future experiments we might be able to duplicate the procedure of irradiation exactly.

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2. The Pharmacopoeia of the United States, Tenth Decennial Revision, Philadelphia, J. B. Lippincott Co., p. 469.

NATURE OF DIET AND LABORATORY PROCEDURE

The experimental animals used in this test were albino rats, aged 3 weeks, from the E. L. Patch Company's stock.

They were fed an experimental ration (Steenbock), containing the following ingredients:

Yellow corn (ground)	76 per cent
Wheat gluten	20 per cent
Calcium carbonate	3 per cent
Sodium chloride	1 per cent

The vitamin B requirements of the animals were met by a yeast tablet containing 50 mg. of yeast concentrate given daily. The animals were kept in individual cages, and the diet and distilled water were constantly before them. This laboratory procedure was followed for a period of forty-two days, at which time the animals were bled and examined roentgenologically and pathologically.

The twenty experimental animals used in this test were divided into five groups. One group, the "control" animals, received the basal diet as outlined. All animals receiving cod liver oil were fed 15 mg. of oil daily. The four groups, the controls and the three groups of experimental animals, were selected so that the groups should be uniform in regard to weight and sex. A fifth group, consisting of the animals that remained from the litters used to supply the animals of the "control" and oil groups, were fed the Sherman Stock Diet (whole wheat flour, 67 per cent and whole milk powder, 33 per cent) and 5 cc. of reconstituted milk a day. Since this diet is ordinarily fed to the stock animals, this group was designated "normal." As a matter of fact, these animals were decidedly underweight at weaning, but a record was made of their growth during the forty-two days that the other animals were under test, and their growth curves have been included. Figure 1 shows that the control animals grew in a satisfactory manner for three or four weeks, and that from that time on they declined rapidly in body weight and developed rickets to such an extent that it was difficult for them to get about the cages. During the same forty-two day period, all animals receiving cod liver oil, whether irradiated or not, grew rapidly and continuously. None of the groups receiving cod liver oil increased in body weight as much as the animals on the normal diet, but perhaps this is not a fair comparison, since the latter animals started at a much lower body weight than those in the group given the oil. In order to facilitate comparison of the growth curves of the different groups of animals, the individual curves of the different groups have been condensed into "composite" curves, which appear in figure 2. As far as weight curves are concerned, the animals receiving cod liver oil irradiated one-half hour and that irradiated two hours did not increase in weight more than

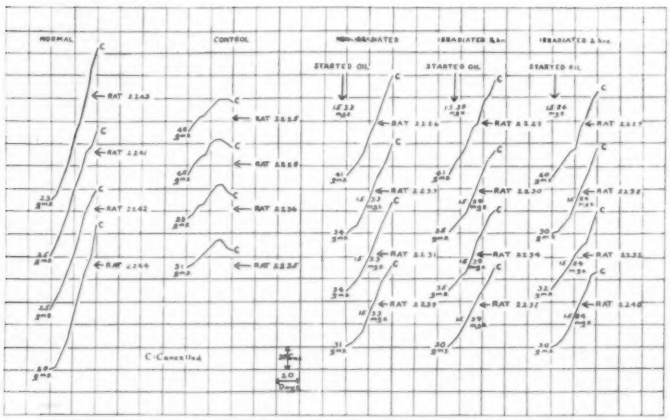

Fig. 1.—Vitamin potency of cod liver oil.

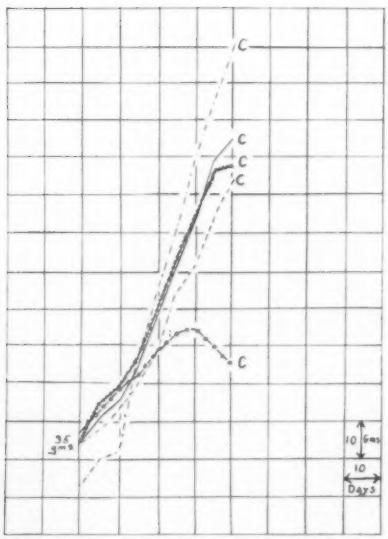

Fig. 2.—Composite curves. The dash and dot line indicates the curves of the normal rats; the dash and circle line, the controls; the solid line, nonirradiated rats; the x line, animals fed oil irradiated one-half hour, and the broken line, animals fed oil irradiated two hours.

the animals receiving nonirradiated cod liver oil. Considered, then, from records of growth, the irradiation of cod liver oil with ultraviolet rays from a quartz mercury lamp does not enhance its vitamin potency.

EXAMINATION OF THE BLOOD

The amount of blood obtained from individual animals was insufficient to make determinations of both calcium and phosphorus. Accordingly, it was necessary to pool the blood of the animals in the different groups. The examination of the blood was made in the laboratory of the Children's Hospital by Dr. Joseph Csapo. He measured the concentration of calcium in the serum by the Kramer [3] method, with 2 cc. of serum, and the inorganic phosphorus concentration in the serum by the method of Fiske,[4] using 1 cc. of serum. Table 2 shows that the calcium content of the blood was fairly constant for the different groups of animals. The diet supplemented with nonirradiated oil gave the highest

TABLE 2.—*Calcium and Phosphorus Content of Blood Serum*

Nature of Diet and of Oil	Calcium in Mg. per Hundred Cubic Centimeters	Phosphorus in Mg. per Hundred Cubic Centimeters	Product of Calcium and Phosphorus
Normal diet	10.8	8.9	96.12
Control diet	....	6.78	.....
Nonirradiated	14.8	5.88	87.02
Irradiated 30 minutes	12.0	7.27	87.24
Irradiated 2 hours	11.8	6.06	71.51

blood calcium. The blood from animals receiving irradiated cod liver oil contained less calcium than that of animals fed nonirradiated oil, and the calcium content decreased with increased irradiation. Consequently, so far as these experiments are concerned, the irradiation of cod liver oil lowered its value for increasing the calcium content of the blood.

The results obtained for blood phosphorus were somewhat erratic. For instance, it is difficult to explain why the phosphorus content of blood serum from animals fed oil irradiated one-half hour should be higher than that of animals fed nonirradiated oil or oil irradiated two hours.

The products of the milligrams of calcium and the milligrams of phosphorus per hundred cubic centimeters of blood serum for four groups of animals have been plotted as a curve. Since the calcium content of the blood serum of the "control" group was not determined, no data for this group appear in this curve. It will be noted on referring

3. Kramer, Benjamin; and Tisdall, F. F.: J. Biol. Chem. **47**:475 (Aug.) 1921.
4. Fiske and Subbarrow: J. Biol. Chem. **66**:375, 1925.

to figure 3 that the value for oil irradiated thirty minutes was the same as that for nonirradiated oil and, further, that the value for oil irradiated two hours was materially lower than that of the original oil. In general, the results of the analysis of the blood show that the antirachitic value of the cod liver oil under consideration was not increased by irradiation with ultraviolet rays for thirty minutes and that the antirachitic potency of the oil was decreased when it was irradiated for two hours.

ROENTGENOGRAPHIC EXAMINATION

Figures 4, 5, 6, 7 and 8 show the results of the roentgenographic examination.

PATHOLOGIC REPORT

Method.—Examination of the long bones of each group of experimental animals was made. For the sake of comparison, identical sections through the

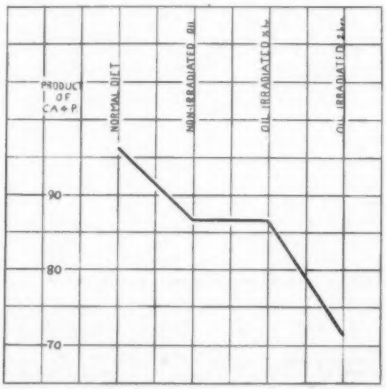

Fig. 3.—Calcium and phophorus content of blood serum.

femora were chosen for microscopic study, as more nearly uniform preparations of these bones could be obtained than of the small bones of the wrist or ankle. Such descriptions as pertain to the femora are equally applicable to the small bones of the wrist and ankle, and it may be assumed that the lesions in these small bones tend to be more marked than the actual lesions under discussion.

GROUP 1 (fig. 9).—*Control animals on a normal full-balanced diet.*

Sections through the femora examined microscopically did not show evidence of any change of the type associated with deficiency disease. There was a normal line of ossification, and the cartilaginous junction was uniform in appearance. The bone marrow was normal (fig. 9).

GROUP 2 (fig. 10).—*Control animals on rachitic diet.*

Sections through the long bones of this group of animals showed a uniform lesion of the type usually described as rachitic. There was marked thickening of the epiphyseal junction, with marked irregularities in the cartilage and bone. The bony trabeculae were increased in thickness but were decreased in density, as evidenced by their irregular staining reactions and the imperfect development of the canaliculi. The cartilage showed marked variation in the size and dis-

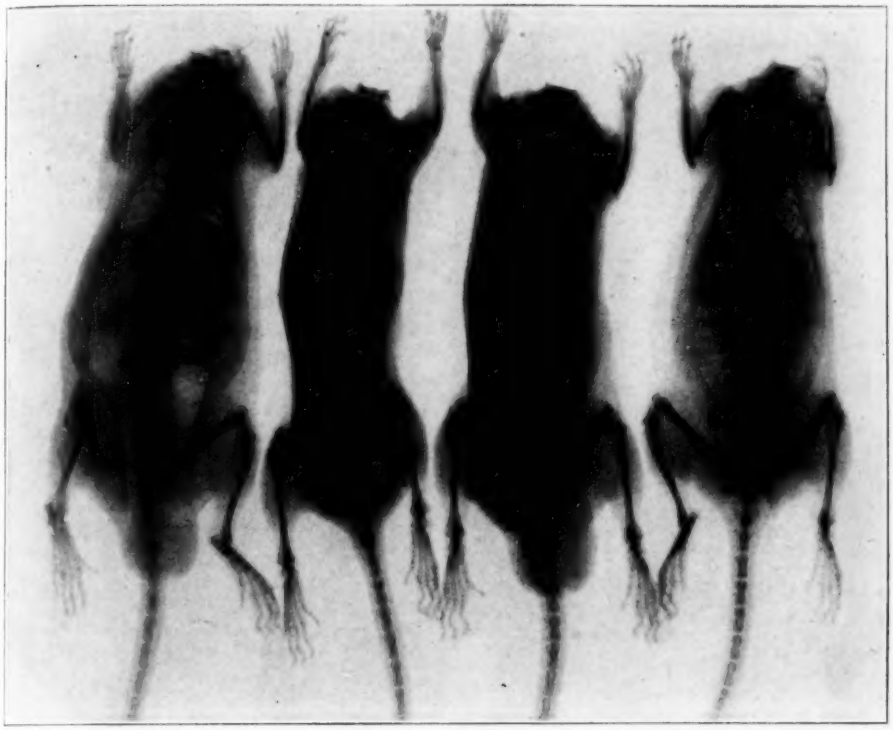

Fig. 4.—Normal rats. The bones do not show any evidence of rickets.

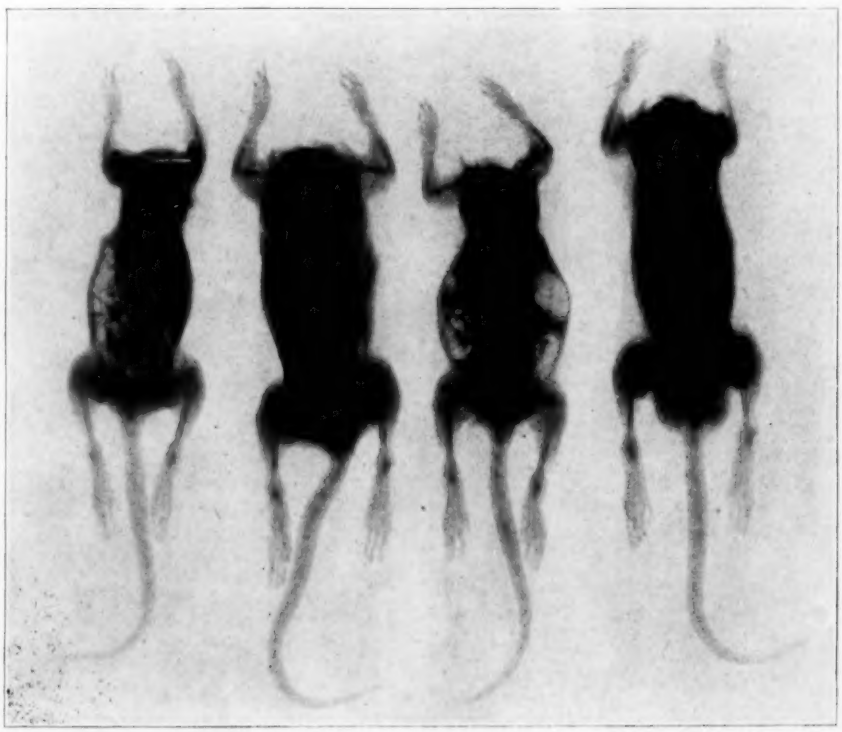

Fig. 5.—Control rats. The bones show severe rickets. The shafts of the bones appear atrophied, and there is marked flaring of the metaphyses, with a ragged, hazy appearance.

Fig. 6.—Rats receiving nonirradiated oil. Examination did not show any evidence of rickets.

Fig. 7.—Rats receiving oil irradiated one-half hour. The bones do not show any evidence of rickets. The appearance is practically the same as that in figure 3.

tribution of the nuclei. The intercellular matrix likewise was variable in density, in places approaching myxomatous degeneration. The marrow was replaced near the epiphyseal junction by fibrous tissue and newly formed blood vessels. There was a poorly developed "white line" of calcification (fig. 10).

GROUP 3 (fig. 11).—*Animals on control rachitic diet with the addition of nonirradiated cod liver oil.*

Sections through identical bones examined microscopically showed essentially normal structure and composition. The bone trabeculae were small and were uniform in their staining reaction. The epiphyseal line was straight with little

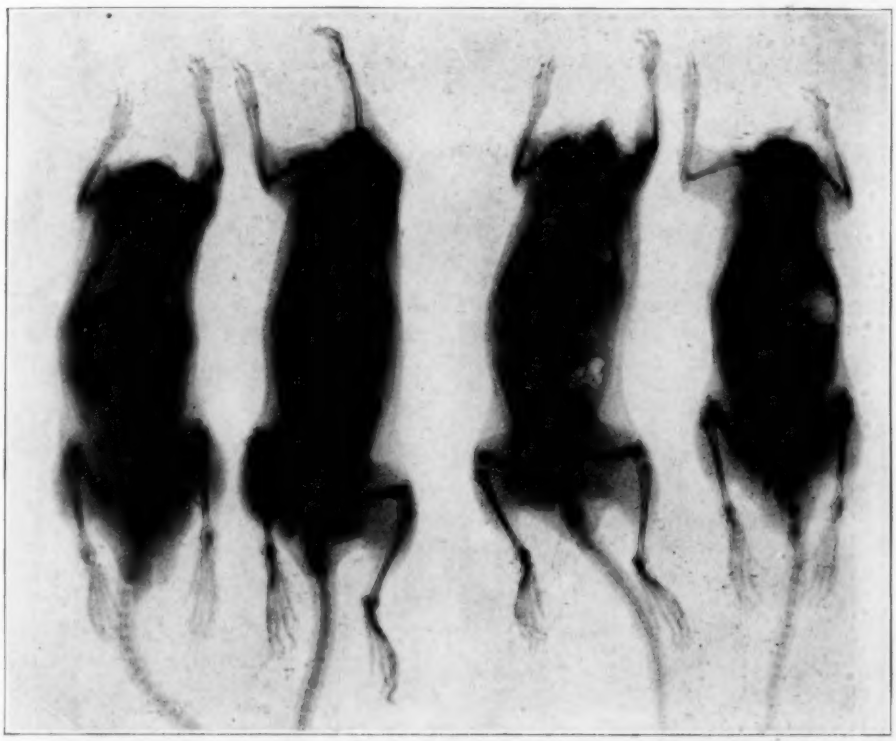

Fig. 8.—Rats receiving oil irradiated for two hours. The bones show the slight changes of rickets. The metaphysis has a hazy appearance, and the epiphyseal line is not clean cut as compared with the normal.

variation in the appearance of the cartilage cells. There was no degeneration of the stroma, and the marrow cavity itself appeared essentially normal (fig. 11).

GROUP 4.—*Control rachitic diet with the addition of cod liver oil irradiated for one-half hour.*

Sections through the long bones in this group showed practically no variation from the preceding group. There was individual variation in each of the two groups, but it was so slight as not to be differentiated microscopically as a consistent characteristic and, indeed, individual bones from group 3 showed as marked changes as those in group 4.

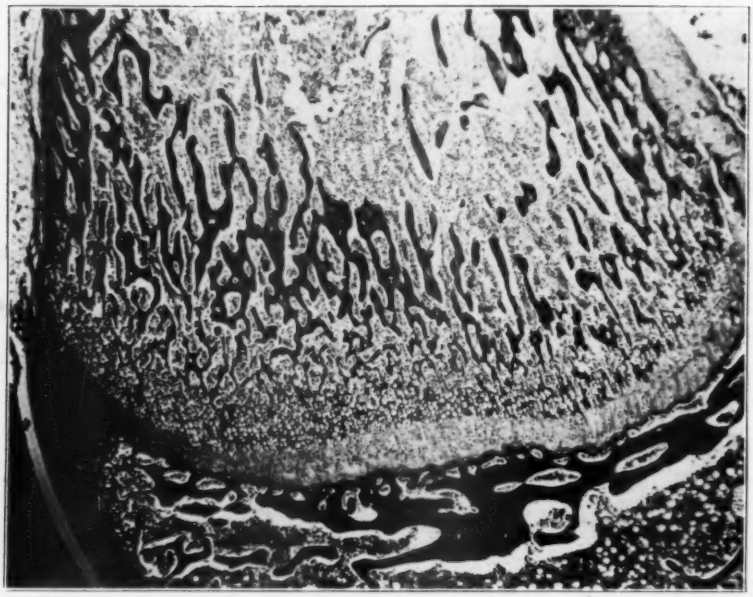

Fig. 9.—Microscopic section through femora of rat from group 1 (control animals on a normal balanced diet).

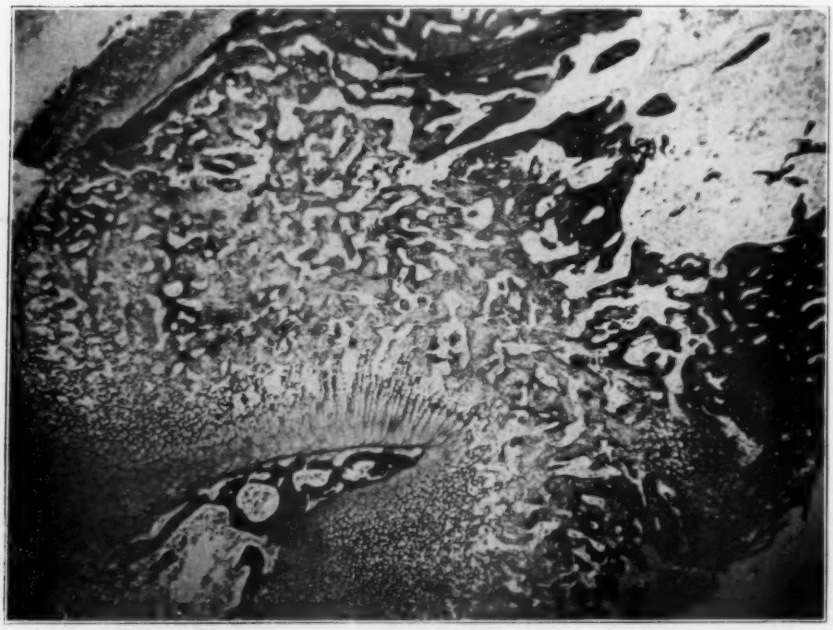

Fig. 10.—Microscopic section through long bone of rat from group 2 (control animals on a rachitic diet).

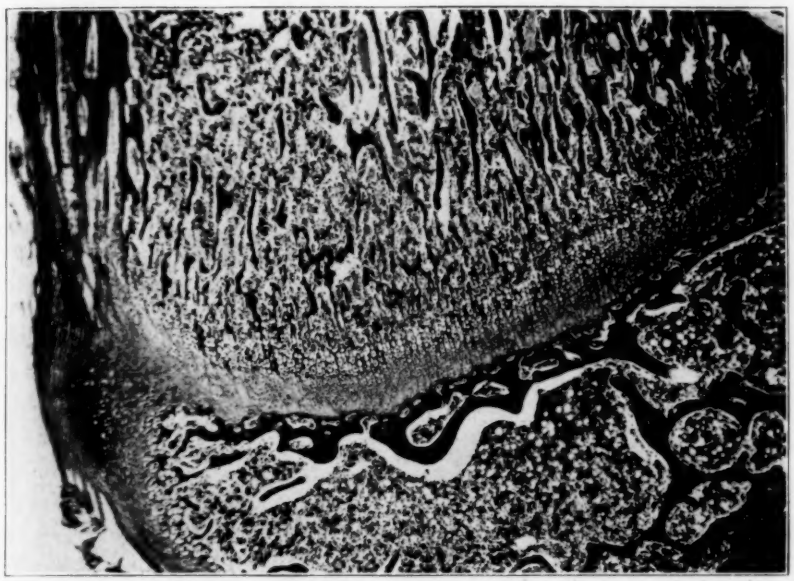

Fig. 11.—Microscopic section through bone of rat from group 3 (animals on control rachitic diet with the addition of nonirradiated cod liver oil).

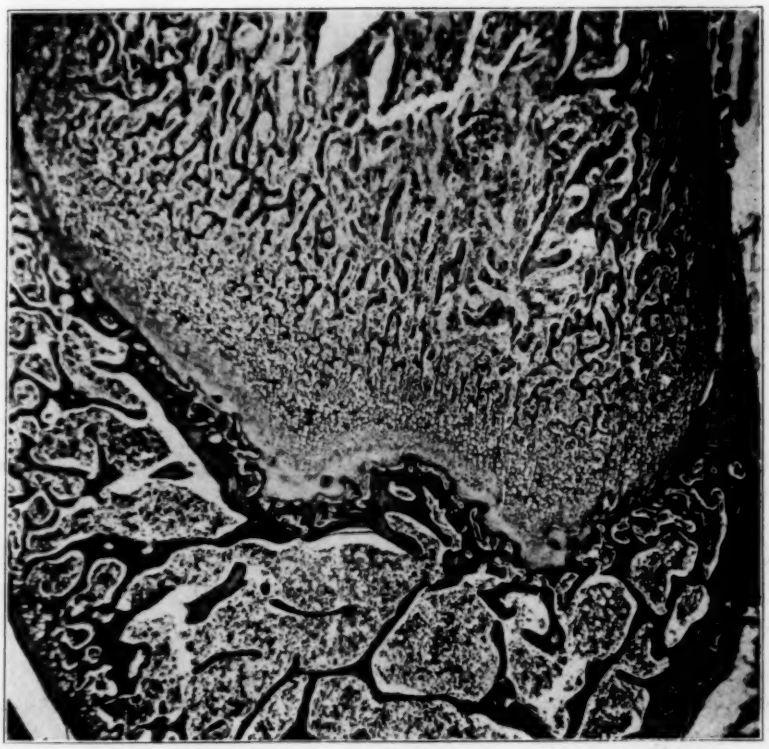

Fig. 12.—Microscopic section through bone of rat from group 5 (animals on the same basic diet plus cod liver oil irradiated for two hours).

GROUP 5 (fig. 12).—*Animals on the same basic diet plus cod liver oil irradiated for two hours.*

Sections through similar bones showed slight histologic changes, which could be interpreted as of a rachitic character. There was more or less variation in the epiphyseal line, in respect to the cartilage particularly. This stained fairly uniformly but showed some irregularity with atypical nests of cartilage cells. The bony trabeculae similarly showed some slight increase in size and variation in staining reaction over the average, as noted in the preceding two groups, but this was a scarcely demonstrable quantitative difference, and histologically the animals might be considered almost within normal limits. They did, however, show, on the average, more striking variation from the normal than either of the preceding groups (fig. 12).

COMMENT

The sections through the long bones of the various groups of experimental animals suggest that irradiation of cod liver oil over any prolonged period tends to destroy some factor in the oil essential to the prevention of rickets. That this is only relative in importance is seen by the slight variation from the normal in the group of animals thus treated, and perhaps in a large series of animals such variation might prove negligible.

On the basis of these experiments, however, there seems to be no adequate reason for the therapeutic treatment of cod liver oil by ultraviolet rays. There are too many variable factors to be taken into consideration, however, to draw any definite conclusions from such a small group of animals.

SUMMARY

A comparison has been made of the antirachitic potency of a medicinal cod liver oil before and after irradiation with ultraviolet rays from a quartz mercury vapor lamp. The oil was irradiated under carefully controlled experimental conditions for thirty minute and two hour periods.

The antirachitic potency of the irradiated and nonirradiated oils was judged by feeding tests with young albino rats. The diagnostic features considered were growth curves, blood calcium and phosphorus, roentgenograms and pathologic examination. The results obtained by these four methods of examination were fairly consistent for each of the five groups of animals.

In general, the results of this study show that the irradiation for thirty minutes of a cod liver oil potent in vitamins does not enhance its antirachitic potency and that irradiation for two hours noticeably decreases its antirachitic activity.

THE EPIPHYSEAL CHANGES IN THE DIAGNOSIS OF SCURVY*

A. B. SCHWARTZ, M.D.
MILWAUKEE

The finer diagnostic features of infantile scurvy have been frequently overlooked, probably due to the fact that students of the disease have been primarily engaged with its hemorrhagic manifestations. Pediatric as well as roentgenologic texts usually exhibit roentgenograms of the femur with the heavy transverse line at its distal end and the subperiosteal hemorrhage as the essential features of scurvy. Though these are indeed unmistakable evidences of the scorbutic state, roentgenologically visible subperiosteal hemorrhage is comparatively infrequent. The heavy transverse line, the so-called "white line" of Fraenkel, has therefore been the deciding element in the roentgenogram. Focusing all our attention on it, we have frequently overlooked conspicuous signs equally characteristic of scurvy. In studying a large series of roentgenograms taken of a group of infants, I was impressed with the great variability of the photographic material. In any given pathologic condition, this may be due as much to the rapidly changing morphologic response of the infantile structure as to differences, to say nothing of inadequacies, of the present technical methods. It is therefore important that every possible distinguishing mark that will lend accuracy to the clinical judgment be utilized.

The admirable contributions of Wimberger [1] in the past few years have revealed the need of a nicer interpretation of the roentgenograms. His studies enable one to correlate the pathologic anatomy of the disease with the graphic evidences seen in the roentgenograms of scorbutic extremities. To make these evidences more intelligible, it is well to hold in view the essential nature of the changes seen in scurvy. These are an almost normal bone resorption with a lack of normal bone regeneration.[2] This results in a diminished density of bone structure showing itself in the thinned cortical layer, in the ground-glass appearance of the spongiosa, and, what is most characteristic, in an area of diminished density visible immediately back of the diaphysis. This area was first identified by Lehndorf as representing the so-called "gerüstmark" of

* Received for publication, June 20, 1927.

* From the Milwaukee Children's Hospital.

1. Wimberger, Hans: Klinisch-radiologische Diagnostik von Rachitis, Skorbut und Lues Congenita im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **28**:264, 1925.

2. Hess, A. F.: Infantile Scurvy, in Abt, I. A.: Pediatrics, 1923, vol. 2, p. 849.

Schödel and Nauwerck, an area composed of loosely constructed fibrillar tissue. The complete absence of bone regeneration in this area may result in breaks in the continuity of the cortical layer itself, so that the diaphysis may appear entirely separated from the shaft (fig. 1). Wimberger believes that what has usually been regarded as epiphyseal separations are frequently intrametaphyseal separations through this area of diminished resistance. Fraenkel recalls that Barlow himself had noted that what are called epiphyseal separations are really infractions of the diaphyseal structure.[3]

Fig. 1.—*A*, gerüstmark; *B*, break in cortex separating diaphysis from shaft and spurring of diaphysis; *C*, subperiosteal hemorrhage.

While not always present, when noticeable, the area of diminished density is in striking contrast with the most familiar roentgenologic sign of scurvy—the Trümmerfeld zone. This term, first used by Fraenkel in describing the well known shaggy band of increased density at the epiphyseal border, is well chosen, because it not only appropriately portrays the "lack of proper and orderly invasion of the cartilage columns"[4] at this point but also identifies a zone in which several characteristic phenomena of scurvy appear. It is here that one finds the laterally projecting spurs from which areas of subperiosteal hemor-

3. Fraenkel, E.: Die Moller-Barlowsche Krankheit, Fortschr. a. d. Geb. d. Röntgenstrahlen, 1908, vol. 18.

4. MacCallum: Text-Book of Pathology, ed. 2, 1922, p. 921.

rhage seem often to originate (fig. 1). In severe cases of scurvy, the chaotic Trümmerfeld zone may be entirely missed. In one of the series observed at the Milwaukee Children's Hospital, in which multiple epiphyseal separations occurred, this was the case (figs. 2 and 3). Reyher is of the opinion that in such instances the bony tissue becomes fragmented and disintegrates into the surrounding parts.

One of the most obvious manifestations in the roentgenograms of scurvy, and one which has received scant attention in American medical literature, is the state of the epiphyseal body itself. Incident to the excess of resorption over bone apposition, the same process as

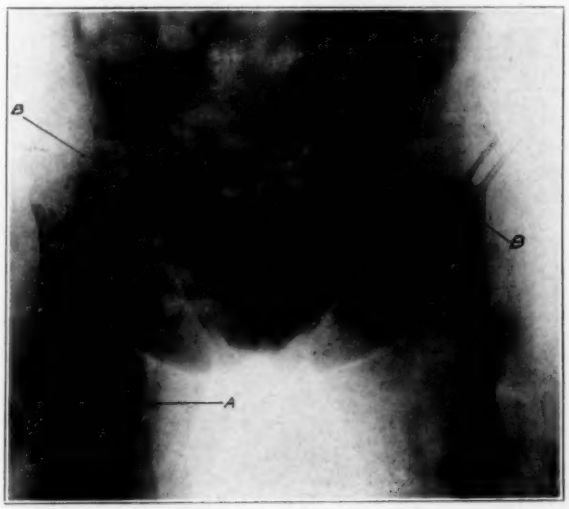

Fig. 2.—*A*, subperiosteal hemorrhage; *B*, epiphyseal or intrametaphyseal separation.

occurs at the metaphyseal line of the long bone, the center of the epiphyseal body itself becomes rarefied and the marginal circumference develops its own Trümmerfeld, the contrast presenting a well-defined ring of greater density around the shadowy central structure (fig. 4). In every instance of scurvy seen in the series studied at the Milwaukee Children's Hospital, comprising all patients entered with the diagnosis for the past five years, this sign is noticeably evident. In the shaggy diaphyseal structure plus the epiphyses exhibiting this heavy bordered contour, one possesses the two signs that are not alone diagnostic from the roentgenologic standpoint but which coincide more regularly with the clinical data in the questionable case. This peculiarity of the epiphyses also affords an additional point of differentiation between the occasional instance of syphilitic osteochondritis, which with

a gummatous infiltration of the metaphyseal ends may greatly resemble the area of diminished density adjoining the Trümmerfeld line of scurvy. Since these two diseases may indeed be the subject of conflicting opinion, it is well to recall that the characteristic bony changes of congenital syphilis practically confine themselves to the period below 4 months, while scorbutic manifestations are not commonly noted before the sixth month—in the present series never before the eighth month. The enormous periosteal scaffolding seen in the syphilitic

Fig. 3.—*A*, intrametaphyseal separation, also showing the absent Trümmerfeld zone; *B*, dimly visible Trümmerfeld and intrametaphyseal separation; *C*, Trümmerfeld at distal end of femur.

subject does not occur in the scorbutic bone, though it is conceivable that a severe subperiosteal hemorrhage may simulate such thickening.

What is occasionally puzzling is the differentiation of rickets and scruvy. The rachitic osteoid zone may greatly resemble the area of diminished density seen beneath the Trümmerfeld of scurvy. Here again, the epiphyseal structure contributes a point of differentiation. The fuzzy, indistinct, contourless margin of the rachitic epiphysis is entirely different from the well defined margin in the scorbutic

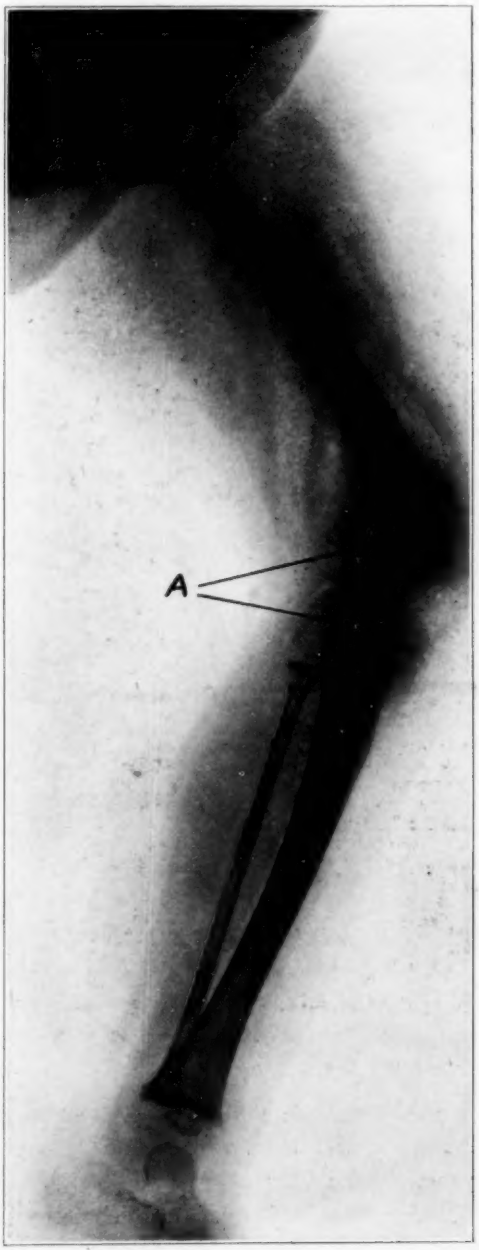

Fig. 4.—*A*, heavy ring around epiphyseal structure corresponding to Trümmerfeld zone of long bone. Rarefied center corresponding to area of decreased density seen directly below diaphyseal line in shaft.

epiphysis. This is well illustrated in Pelkan's interesting contribution to the subject.[5]

The state of the epiphysis not only has its immediate diagnostic importance, but, as Wimberger has shown, also remains a tell-tale evidence of the bony changes for some time afterward. All patients with the diagnosis of scurvy seen during the past five years at the Milwaukee Children's Hospital were returned for roentgenograms during the past few months. The epiphysis at the distal end of the

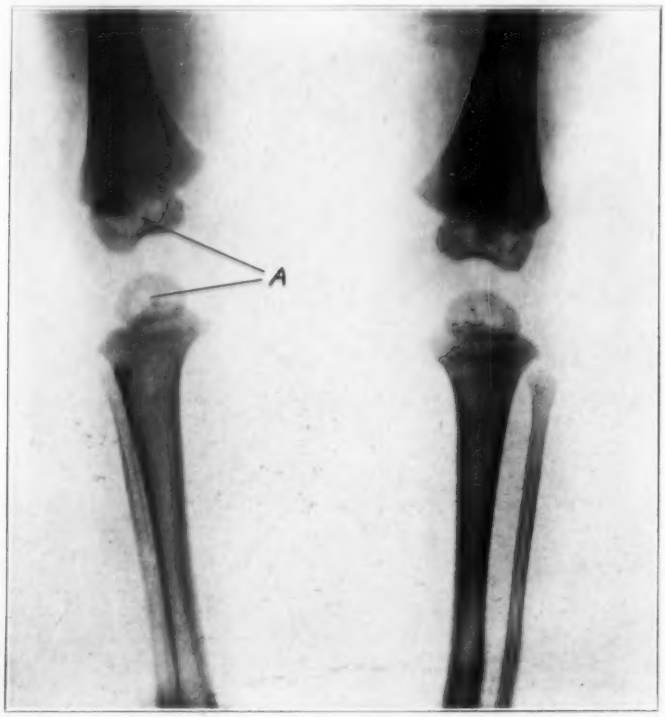

Fig. 5.—Appearance eighteen months after healed scurvy. *A*, inset in epiphyseal body which represents original epiphyseal structure present during height of acute scorbutic manifestations.

femur presents a roentgenologic sign seen in no other condition. The previously rarefied epiphyseal body, with its distinctly outlined circumscribing ring, is seen in the later epiphyseal structure as a pale inset. Around this inset, the subsequent bony growth of normal density appears as a ringed contour. The greatest growth of new bone occurs laterally and toward the joint surface, the least growth on the side in apposition

5. Pelkan, K. F.: The Roentgenogram in Early Scurvy, Am. J. Dis. Child., **30**:174 (Aug.) 1925.

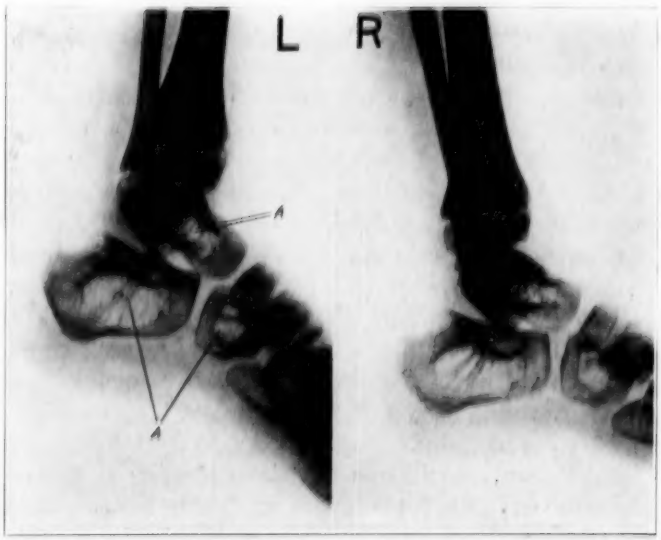

Fig. 6.—Appearance four and one-third years after healed scurvy. *A*, inset in epiphyseal structure—os calcis, astragalus and cuboid.

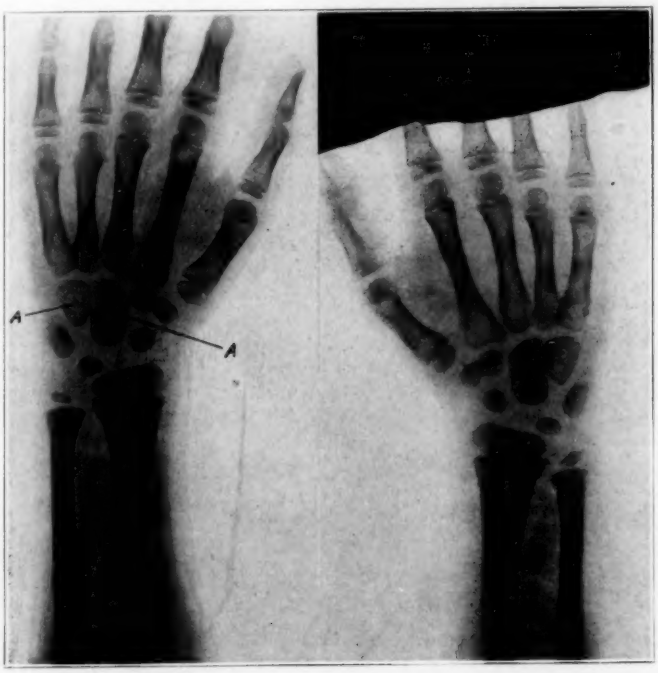

Fig. 7.—Appearance four and one-third years after healed scurvy. *A*, inset in epiphyseal structure—os capitatum and os hamatum.

to the long bone. The coarsely dense structure of the later bony growth appears in such contrast to the washed out appearance of the previous epiphysis that the epiphyseal structure appears to have a double contour (fig. 5). This peculiar characteristic of the postscorbutic state apparently remains for many years.

The most striking example of this manifestation (fig. 6) was seen in a patient of whom the subsequent roentgenograms were taken four years and three months after discharge from the hospital. In a private patient treated for scurvy seven years ago, the present roentgenograms, which were furnished by Dr. G. W. Stevens, roentgenologist, Columbia Hospital, still show a slight residue of this interesting condition in the epiphysis at the distal end of the femur. In occasional instances, one can also discern faint remains of the transverse Trümmerfeld line in the shaft of the long bone. As the knee offers the best place for the roentgenologic study of acute scurvy, it likewise is the best place to view the later insets. It is interesting to observe in figure 6 that such insets are visible at the carpus and tarsus only in the epiphyses that had reached ossification. In the carpus, the os capitatum and the os hamatum—the only two carpal centers present at the age of 2 years when the patient had the acute symptoms—exhibit the inset. In the tarsus, these insets are seen in the os calcis, the astragalus and the cuboid.

GENERALIZED EDEMA OF UNDETERMINED ETIOLOGY

REPORT OF AN UNUSUAL CASE *

WILLIAM L. ROST, M.D.
NEW YORK

Generalized edema associated with renal, cardiac and nutritional disease and with certain diseases of the blood is commonly recognized; the so-called angioneurotic edemas are also well known, but generalized edema not associated with any of the disorders mentioned is not so frequent and may even escape attention.

Constatt,[1] in 1856, classified certain forms of hydrops not readily explained on the basis of the then known etiologic factors, as a manifestation of pathologic changes of the skin.

Wernich [2] reported an interesting case in which a complete autopsy failed to reveal any pathologic change that might explain the cause of the edema.

In a comprehensive review, Wagner [3] reported his observations in eight cases of generalized edema; six occurred in children ranging in age from 22 months to 12 years; three children recovered and three succumbed. The following symptoms occurred in his cases: The character of the onset of the illness varied in each child; all the patients were pale and gave the impression of being seriously ill; the edema was most pronounced in the lower half of the body; some fluid was present in the serous cavities; the pulse and temperature varied only a little from the normal; a sufficient number of examinations of the urine were made to exclude chronic interstitial nephritis. The complications were bronchitis, pneumonia and dysentery. Postmortem examination failed to show any causative factor for the edema.

One carefully anayzing Wagner's cases, one can readily conceive that they might well be explained on the basis of a nutritional disorder complicated by an infectious process.

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* Received for publication, May 31, 1927.

* From the Pediatric Service of the Mt. Sinai Hospital.

1. Constatt: Handbuch d. med. Klin. **3**:925, 1856.

2. Wernich, A.: Zur Pathogenese des Essentielle Hydrops, Deutsches Arch. f. klin. Med. **6**:622, 1869.

3. Wagner, E.: Die Sogenannte Essentielle Wassersucht, Deutsches Arch f. klin. Med. **41**:509, 1887.

More recently, Meyer-Bisch [4] reported four cases of his own and cited three by other observers; a summary of his observations is worthy of recording here:

1. All the patients had generalized edema and showed changes in the quantitative output of urine.
2. The urine was free from albumin and casts.
3. The blood pressure was normal.
4. There was no cardiac enlargement.
5. There was no anemia.
6. The serum albumin was reduced in three cases.
7. The sodium chloride in the blood was normal in three cases; in one, it was normal or low or high at different times without discernible cause.
8. The water balance in two cases was practically normal.
9. Gastric analysis was normal.
10. Two patients showed polyglandular disturbance (retarded genital development and sparse pubic hair).
11. The addition of sodium chloride in two cases resulted in a sharp rise in weight.

It was Meyer-Bisch's opinion that the edema present in these cases was "the result of a damage to the tissues and an imbalance of the salt and water metabolism."

REPORT OF CASE

History.—G. H., a girl, aged 6, was admitted to the pediatric service of the Mt. Sinai Hospital, Jan. 23, 1925, and was discharged improved, June 11, 1925.

Previous History.—She had had frequent attacks of sore throat up to about one year previously, when her tonsils had been removed; she had never had measles, scarlet fever, diphtheria, asthma, hay-fever or urticaria, and a number of skin tests for protein sensitization were negative.

Present History.—Twelve weeks prior to admission to the hospital it was first noted that the eyelids and upper lip were swollen; this swelling had varied in intensity from time to time but had never entirely disappeared; there were no other symptoms. She felt well and continued her normal activities up to two weeks previously, when she complained of some dyspnea and slight pain in the left hip; the temperature was not elevated, and she was not confined to bed; at no time were headache, visual or urinary disturbance, cough, cardiac consciousness or edema of the lower extremities present.

Physical Examination.—On admission, the child weighed 22.5 Kg. The sitting height was 63 cm. and the standing height, 117 cm. She was fairly well nourished, and was not dyspneic or acutely ill. There was edema of the face, eyelids, trunk and thighs; the superficial lymph nodes were not enlarged, and no deformities or nodules were present; the skin over the trunk and abdomen felt thick and velvet-like; the nose and throat were normal. Over the thorax anteriorly, flatness was elicited in the left axilla, merging with the cardiac dulness; breath and voice sounds were diminished; posteriorly both bases were flat, extending

4. Meyer-Bisch, R.: Storungen des Intermediaren Salztoffwechels und ihre Klinische Bedeutung, Klin. Wchnschr. **4**:588, 1925.

upward to the angles of the scapulae, a little higher and more marked on the left side; voice and breath sounds were suppressed; the heart sounds were clear and of good quality, and there was no irregularity; shocks, murmurs or thrills were not heard; the rate was 120 a minute, the left cardiac border merging with pulmonary dulness and the right border 3 cm. to the right of the midsternal line. The spleen was palpable 2 cm. below the costal margin; the abdomen was enlarged, was firm and smooth, and the shifting dulness within the abdomen was demonstrated; the superficial veins were not enlarged, and no tumor masses were felt; the genitalia were normal. The nervous system did not reveal any abnormalities. The eyes were clear; the pupils were equal and reacted to light and in accommodation. No petechiae were present; the fundi were normal. The Pirquet, Mantoux, Schick and Wassermann tests were all negative. On January 26, the blood pressure was 80 systolic and 60 diastolic.

TABLE 1.—*Examination of the Blood*

Date	Hemoglobin, per Cent	Red Blood Cells	White Blood Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Mononuclears, per Cent	Myeloblasts, per Cent	Basophils, per Cent
1/24	100	Normoblast	16,900	62	37	1	..	..
2/24	...	Normoblast	31,000	77	15	5	2	1
2/28	85	5,300,000	.....	..	..	..	..	..
5/ 5	90	4,000,000	22,000	52	48	..	..	..

TABLE 2.—*Blood Chemistry*

Date	Urea Nitrogen	Uric Acid	Creatinine	Cholesterol
1/ 1.....	15.4	3.5	1.0	0.160
3/3).....	15.4	2.5	1.0	0.124

TABLE 3.—*Chemistry of Aspirated Fluid From the Chest*

Date	Urea Nitrogen	Nonprotein Nitrogen	Uric Acid	Creatinine	Cholesterol
3/30.....	12.6	30.0	3.5	1.0	1.106

No tumor cells were found.

On January 28 the blood pressure was 84 systolic; 60 diastolic.

On April 4 the blood pressure was 80 systolic, and 50 diastolic.

Laboratory Examination.—The results of the examination of the blood are shown in table 1.

The blood chemical determinations are shown in table 2.

A culture of the blood was negative. The chemistry of the aspirated fluid from the chest is shown in table 3.

On March 20, the total blood protein was 7.187, of which the albumin was 3.742 per cent and the globulin, 3.445 per cent.

On March 30 the total protein was 7.431, of which the albumin was 3.954 per cent and the globulin, 3.479 per cent.

Urine Analysis.—A total of twenty-four complete examinations were made; the specific gravity varied between 1.020 and 1.030, the average being 1.027; the total output of the urine varied between 275 cc., the lowest, and 850 cc., the highest amount; this depended considerably on the amount of food and water

intake. The output of sodium chloride on admission was 8.95 Gm. in twenty-four hours; a calculated diet, in which 10 Gm. of sodium chloride was administered May 19 and May 20, showed an output of 8.2 Gm. in twenty-four hours and 9.0 Gm. when repeated.

The intradermal saline absorption test required forty-two minutes on admission; when repeated several weeks later, it required forty-five minutes.

The weight curve showed little variation; on admission, the child weighed about 22.5 Kg., and when discharged, 22 Kg.; at no time during the stay in the hospital

Appearance of child having generalized edema without any evidence of cardiac or nephritic disease and no angioneurotic edema.

did her weight decrease more than 2 Kg. and then for about one week during the administration of merbaphen; when the therapy was discontinued, the weight promptly returned to 22.5 Kg.

An Ewald test showed no free hydrochloric acid; the total acidity was 65 per cent.

Electrocardiographic studies showed: February 4, sitting posture, low voltage in all leads, and no preponderance; on the right side, low voltage and no preponderance; on the left side, right ventricular preponderance; April 17, low voltage in all leads and marked tachycardia; April 20, no appreciable change in electrocardiogram on change of posture; simple tachycardia present.

Fluoroscopic examination of the chest on January 28 revealed a homogeneous shadow occupying the region of the heart and evidence of fluid in the costophrenic sinus; the diaphragm was not visible, nor were any cardiac pulsations seen; the posterior lateral view showed practically a clear chest.

On February 24, examination showed an opaque shadow in the mediastinum; the heart shadow was not outlined; the fluid level was high up on the right side anteriorly, but less so on the left side.

Roentgen-ray examination of the accessory sinuses, skull, sella turcica and esophageal region did not reveal any abnormality.

Therapy.—High protein diet, diuretin merbaphen, pituitary, thyroid extract and thyroxin were administered at different times, without any sustained effect on the course of the disease.

The patient was discharged, June 11, 1925; the general condition was improved, the edema somewhat lessened, the chest practically normal, and the heart, except for some enlargement to the right and left, showed no evidence of disorder.

Notes from the Follow Up Clinic.—The child attended the clinic from Oct. 29, 1925, to Dec. 15, 1926. During this time it was found that her general condition remained practically the same as it was when she left the hospital; she attended school regularly except for two weeks when she had an attack of varicella; three roentgen-ray examinations during this time disclosed practically no change.

SUMMARY

A case of generalized edema in a girl, aged 6, a careful study of whom failed to demonstrate the etiology, is reported.

The outstanding features in this case are: The persistence of the edema, the marked well being of the child, change in the ratio of the albumin to globulin in blood, the normal blood chemistry, the urine free from albumin and casts, normal blood pressure and the normal output of sodium chloride. The addition of sodium chloride did not cause an appreciable rise in weight.

COMMENT

The questions that suggest themselves are, What is the cause of this edema? and What symptoms in the case reported might throw some light on the etiology?

Meyer-Bisch is of the opinion that a damage of the tissues and an imbalance of the salt and water metabolism brings about retention of fluid in the tissues. It is my opinion that this imbalance of the metabolism is not primary, but is brought about by some other factor. The case reported did not show any marked change in water retention on the addition of sodium chloride.

Low blood serum may also be a contributing factor in aiding exosmosis of fluid into the interstitial tissues; on the other hand, in cases of nephrosis in which one finds marked edema of the tissues, often a relatively high blood albumin and a correspondingly low blood globulin are found. This condition was present in the case reported without evidence of involvement of the kidneys. The possibility of damage to the endo-

thelial cells of the fine capillaries, brought about by some chemical dissociation in the cell metabolism, must also be considered.

Finally, it is also conceivable that such a condition as the one discussed might occur only in persons with some curious congenital anomaly of the tissues, which makes them more susceptible to generalized edemas.

CONCLUSION

It is apparent that many more cases will have to be studied and observed carefully for long periods of time before any definite information as to the etiology of this disorder can be offered.

PHLYCTENULAR KERATOCONJUNCTIVITIS

ITS ETIOLOGY AND TREATMENT *

HORTON CASPARIS, M.D.
NASHVILLE, TENN.

The success that I have had with a specific form of treatment in phlyctenular keratoconjunctivitis seems to justify a reconsideration of this much written about subject; also, the results may give convincing proof of the causation of the condition. The type of treatment that I shall discuss is not new, but, judging from the results obtained, it is too little used.

ETIOLOGY

I consider a tuberculous focus somewhere in the body as the underlying etiologic factor in phlyctenular keratoconjunctivitis, and I consider phlyctenular keratoconjunctivitis as a local manifestation of hypersensitiveness of the individual to tuberculin. This manifestation is of the nature of an eczema of the cornea and conjunctiva, and tuberculin is the specific protein or substance to which hypersensitiveness has developed.

Further discussion of the etiology will appear later.

DIAGNOSIS

The fact that so many different diseases of the eyes are occasionally diagnosed phlyctenular keratoconjunctivitis indicates that the diagnosis is not always easy. Such conditions as acute catarrhal conjunctivitis (pink eye), injuries to the eye, trachoma, gonococcus conjunctivitis, acute interstitial keratitis, pneumococcus conjunctivitis, Parinaud's conjunctivitis, acute follicular conjunctivitis and excessive exposure of the eyes to ultraviolet rays are at times confused with phlyctenular keratoconjunctivitis. Chronic trachoma and chronic interstitial keratitis are in some respects similar to chronic phlyctenular keratoconjunctivitis; interstitial keratitis, especially, is confused with it.

Phlyctenular keratoconjunctivitis, however, usually produces a characteristic appearance of the patient. Photophobia, although not always marked at the onset, is as a rule the most pronounced symptom. Hence, in bright or moderately bright light, one sees the patient with his arm covering his eyes, or with his head bowed and the eyes closed. If he is in bed, his face is usually buried in the pillow. The photophobia is often extreme, and the child opens his eyes cautiously only when he

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* From the Department of Pediatrics of the Vanderbilt University Hospital.

thinks he is somewhat protected from the light. Blepharospasm may be pronounced. Lacrimation is always present during the active stage. There is little or no pus. Pain is not present except as discomfort caused by light. On the cornea and less often extending onto the bulbar conjunctiva are small whitish patches, slightly elevated, from about 1 to 3 millimeters in diameter, with a skein of dilated capillaries leading up to them. These are the phlyctenules. If they are not present, one often sees the small cloudy areas where they have been. Probably the lesions appear more frequently as small nodules chiefly at the corneal border, and it is the lesion in this region that is more apt to ulcerate.

Fig. 1.—Phlyctenular keratoconjunctivitis, showing protection of eyes because of extreme photophobia.

Here one occasionally sees an ulcer or the scar from an ulcer. In addition to these evidences of localization, there is moderate conjunctival congestion consisting of visibly dilated capillaries. The dilated capillaries are more prominent in the pericorneal region, especially in the more chronic cases. One or both eyes may be involved. Often one eye becomes involved followed in days, weeks or months by involvement of the other. There is a marked tendency to repetition of attacks. Each attack may last only a week or two; in children, however, the condition usually continues much longer, lasting even months or years with only partial remission of symptoms from time to time. With new attacks or with exacerbations, there are usually new phlyctenules. Most of the cloudy areas following these lesions clear completely. Others,

and of course scars from ulcers, remain as corneal defects. These are mentioned because in diagnosis they indicate evidence of previous attacks. In all the patients, the tuberculin reaction has been positive and usually violently so. The intracutaneous tuberculin test is used, and in most instances there is a definite reaction to 0.01 mg. of old tuberculin. The Wassermann test has been negative in every instance.

TREATMENT

Since phlyctenular keratoconjunctivitis is considered as a manifestation of hypersensitiveness of the patient to tuberculin, the treatment consists of at least a partial desensitization of the patient to tuberculin. Old tuberculin is used. Dilutions are made in physiologic sodium chloride solution with one fourth of 1 per cent phenol as a preservative.

Tuberculin Dilution and Dosage

Stock Dilutions of Old Tuberculin		Treatment		
Preparation	Dilution and Quantitative Value	No.	Dosage in Cc.	Dosage (Mg.) of Old Tuberculin
		1	0.1	0.0001
6—4½ cc. carbolized saline ½ cc. no. 5	1: 1,000,000 1 cc.-0.001 mg.	2	0.2	0.0002
		3	0.4	0.0004
		4	0.7	0.0007
		5	0.1	0.001
5—4½ cc. carbolized saline ½ cc. no. 4	1: 100,000 1 cc.-0.01 mg.	6	0.2	0.002
		7	0.4	0.004
		8	0.7	0.007
		9	0.1	0.01
4—4½ cc. carbolized saline ½ cc. no. 3	1: 10,000 1 cc.-0.1 mg.	10	0.2	0.02
		11	0.4	0.04
		12	0.7	0.07
		13	0.1	0.1
3—4½ cc. carbolized saline ½ cc. no. 2	1: 1,000 1 cc.-1.0 mg.	14	0.2	0.2
		15	0.4	0.4
		16	0.7	0.7
		17	0.1	1.0
2—4½ cc. carbolized saline ½ cc. no. 1	1: 100 1 cc.-10 mg.	18	0.2	2.0
		19	0.3	3.0
		20	0.4	4.0
		21	0.5	5.0
1—4½ cc. carbolized saline ½ cc. Old Tuberculin	1: 10 1 cc.-100 mg.	Treatments to be given every three days or twice a week.		

Dark or brown bottles are used, and the dilutions are kept cool when not being used, to prevent the tendency of the solution to deteriorate. For convenience, quarter or half ounce bottles with puncturable rubber stoppers are used. Dilutions and dosage are given in the accompanying table.

A much smaller dose of old tuberculin is given than that which will produce a demonstrable reaction, and the dose is gradually increased to 5 mg. This upper limit was chosen because through experience it was learned that if one stops much short of 5 or 10 milligrams, the sensitiveness of the skin returns fairly quickly, accompanied in some instances by a recurrence of manifestations of disease of the eyes.

The tuberculin is given subcutaneously every third day or, for the convenience of the patient, twice a week. The three day interval was chosen because it was thought advantageous to have a beginning reces-

sion of the previous reaction before the following injection is given. It will be recalled that the height of the tuberculin reaction comes at about the end of two days. The intracutaneous method of desensitization has not yet been sufficiently tried to judge of the relative merits of the two methods. The intracutaneous injection has the disadvantage of producing more discomfort both during and after administration. An attempt is made to graduate the dosage so that there will be no demonstrable reaction to any individual injection. When a reaction does occur, however, the following dose is either the same as the previous one or smaller, depending on the extent of the reaction. A reaction may assume the form of tenderness only or tenderness, redness and swelling at the point of injection. Or, what is most significant in connection with the idea of tuberculin being the specific sensitizing substance, the reaction occasionally assumes the form of a flare-up in eye symptoms.

Fig. 2.—Phlyctenular keratoconjunctivitis, showing extreme photophobia, lacrimation and blepharospasm.

During two or three such reactions, a new phlyctenule has appeared; this occurred after the paient had previously shown definite improvement. These severe reactions have come most often when through mistake several doses of tuberculin have been skipped and too large a dose has been given, such as 0.01 mg. instead of 0.001 mg. Occasionally, such a reaction occurs in the regular course of treatment. Then it may be assumed that the dosage was increased too rapidly for that particular patient, or, what is more likely, that there was a coincident release of tuberculin from some focus in the body; this, added to the injected tuberculin, was sufficient to produce a flare-up in the eye manifestations. Similar irregularities occur when one attempts to desensitize against some specific pollen during the season when that particular pollen is in the air.

RESULTS

During the past year and a half, eighteen patients with phlyctenular keratoconjunctivitis have been treated with tuberculin. In every instance, partial relief of symptoms has begun immediately. In some cases, even the intracutaneous tuberculin injected as a test has given some relief. In all except one or two instances, in which there was marked blepharospasm, most symptoms have disappeared before the four injections of a 1:1,000,000 dilution have been completed. In every case complete disappearance of symptoms and signs was obtained (except scars) as desensitization proceeded. The intracutaneous tuberculin test was repeated at the end of the course of treatment, using 0.1 mg. of tuberculin, and it was found that the patient's skin reacted slightly or not at all to this dose.

In all patients except one, there has been a marked gain in weight during treatment. The four adults that were treated volunteered the

Fig. 3.—Phlyctenular keratoconjunctivitis, showing typical facial expression in marked photophobia.

information during treatment that they felt better than they had for months.

There has been one recurrence after seven months in a small child, aged 2 years, who has remained at home where there is open tuberculosis. The recurrence was in the other eye, and on examination it was found that he had again become violently sensitive to tuberculin. Even though his symptoms had been present three weeks in the last attack, they began to clear after the first injection of tuberculin. After three injections, the symptoms had disappeared.

COMMENT

It has been mentioned that in all the patients there has been a positive tuberculin reaction. It has been my experience however, either that the amount of demonstrable tuberculous involvement has been small or that the patient has his tuberculosis well under control. One rarely

sees phlyctenular keratoconjunctivitis in a tuberculous patient who is doing badly. This probably lends some support to Krause's view that allergy and immunity go hand in hand.

The question will immediately arise, "If phlyctenular keratoconjunctivitis is a tuberculous manifestation, why does it not occur more often, since tuberculosis is so widespread"? It is my belief that individuals who develop phlyctenular keratoconjunctivitis belong to that group, the members of which are hypersensitive to various "foreign proteins." For example, one who develops phlyctenular keratoconjunctivitis develops it as a manifestation of hypersensitiveness to tuberculin,

Fig. 4.—Appearance after treatment with tuberculin. The patient had had phlyctenular keratoconjunctivitis for nine months and was told that her left eye would have to be removed.

just as another may develop hay-fever as a manifestation of hypersensitiveness to ragweed. In fact, in most of the cases described, there has been a personal or family history of urticaria, eczema, hay-fever or asthma. The most common lesion in the patients themselves has been seborrheic eczema. Thus, the peculiar incidence of phlyctenular keratoconjunctivitis may be explained.

There are still many who believe that phlyctenular keratoconjunctivitis is the result of foci of infection, such as infected sinuses, teeth, tonsils, adenoids or of poor diet and poor hygiene, and that when such defects are corrected phlyctenular keratoconjunctivitis will clear up. I

recognize the tendency to spontaneous clearing in early phlyctenular keratoconjunctivitis of children and in some cases in adults, but in most of the patients the condition has been chronic, having been present for months or years. With local therapy or a slight improvement in food or hygiene, there is usually a remission of symptoms, but new phlyctenules often appear in a week or two or the other eye becomes involved. Several of the patients had been under the constant care of ophthalmologists, and about every variety of therapy except tuberculin had been tried. In two instances, the patients had been told that removal of the involved eye would be necessary in order to save the good eye.

I do not wish to minimize the value of general corrective measures because they are at the bottom of healthy living and are the fundamentals on which the treatment of tuberculosis is based. If one heals or arrests tuberculosis, one cures all of its manifestations. But this is a slow way of clearing up phlyctenular keratoconjunctivitis, and one is not justified in prolonging the condition with the frequent coincident irreparable damage to the cornea, when treatment with tuberculin offers such rapid relief.

Treatment with tuberculin will protect against recurrence sufficiently long in most instances to enable one by general supportive measures to procure healing or arrest of the underlying tuberculous focus. If there is doubt about the care the patient is to receive, it may be of value to give an injection of tuberculin once a week or every two weeks after routine treatment has been finished, to prevent the patient's return to a hypersensitive state.

SUMMARY

All of the patients with phlyctenular keratoconjunctivitis reacted to tuberculin intracutaneously. Usually they showed a minimal amount of tuberculous involvement elsewhere.

Eye symptoms in every instance began to clear immediately when treatment by desensitization to tuberculin was begun. Response to extraordinarily small amounts of tuberculin was marked.

Exacerbations in eye symptoms in some instances occurred during the course of desensitization, apparently as the response to an overdose of tuberculin.

Tuberculin treatment offers protection against recurrence of attacks for a sufficient length of time to procure through general measures the arrest of the underlying tuberculous focus.

The peculiar incidence of phlyctenular keratoconjunctivitis may be explained by assuming that those who develop the disease belong to that group of individuals who are hypersensitive to some "foreign protein."

CONCLUSIONS

1. Phlyctenular keratoconjunctivitis is in all probability a local manifestation of hypersensitiveness of the patient to tuberculin and a tuberculous focus somewhere in the body is the underlying etiologic factor.

2. This manifestation, phlyctenular keratoconjunctivitis, can readily be made to disappear by at least partially desensitizing the patient to tuberculin.

NONTUBERCULOUS FIBROSIS OF THE LUNGS*

H. HARRIS PERLMAN, M.D., PH.D.
Instructor in Diseases of Children, Jefferson Medical College
PHILADELPHIA

The discovery of the tubercle bacillus by Robert Koch in 1882 made possible the extensive and varied studies which have since disclosed much that is important and interesting concerning obscure tuberculous lesions. Before Koch's epoch making research, many of the older clinicians assumed pulmonary hemorrhage to be an inevitable sequence of tuberculosis. Faulty postulation of the nature indicated was not altogether unjustifiable in view of the fact that microscopy and bacteriology were in their infantile stages of development.

Andral, Addison, Morgagni, Jacourd, Handfield, Jones, Sutton and Clark are included among the investigators who recognized nontuberculous fibrosis of the lungs as a distinct entity.

The report of the case that follows deals with that form of fibrosis which is independent of the tubercle bacillus. Without having been initiated fully into the characteristic diagnostic problems, one reaches the decision largely by the process of exclusion and conditions are often wrongly labeled "tuberculosis."

TYPES OF PULMONARY FIBROSIS

From a pediatric standpoint, conditions producing fibrosis of the lungs may be grouped conveniently as follows:

1. Tuberculous
2. Nontuberculous
   - (*a*) Infections of the respiratory tract following pneumonia, pertussis, measles and influenza.
   - (*b*) Syphilis.
   - (*c*) Fungus infections (actinomycosis, streptothricosis).
3. Extraneous
   - (*a*) Foreign bodies.
   - (*b*) Pneumonkoniosis.

ETIOLOGY

In Atkinson's[1] study, out of 1,000 consecutive admissions to the outpatient department at the hospital for sick children, Great Ormond Street, London, fifteen cases were diagnosed as nontuberculous fibrosis

* Received for publication, June 15, 1927.
* Read before the Philadelphia Pediatric Society, May 10, 1927.

1. Atkinson, Dorothy W.: Am. J. M. Sc. **170**:693 (Nov.) 1925.

of unresolved pneumonia. In twenty children with the condition reported by Atkinson, the ages ranged between 18 months and 14 years. It is interesting to know that in fourteen of the twenty children the onset of the disease occurred during the first five years and in the remainder between 5 and 10 years. In seven of Atkinson's cases, the condition could be traced to a preceding pertussis complicated with bronchopneumonia. In six, the symptom dated to pneumonia of unknown origin. In two, the condition followed a severe attack of chickenpox. In five, the exact relationship to previous infection was not known, but in each case there was a history of repeated severe respiratory infections.

The infection is essentially one of early life, traceable in most instances to bronchopneumonia. It is characterized by great chronicity, which finally eventuates in physical impairment.

Bacteriologically, one finds as common offenders the pneumococcus, the influenza bacillus, *Micrococcus catarrhalis* and various types of streptococci. The tubercle bacillus is dominantly conspicuous by its absence.

Herbert [2] states that nontuberculous fibrosis is the commonest chronic pulmonary disease of childhood and points out the early age at which the process starts. He places the onset usually in the second or third year following whooping cough or measles with bronchopneumonia. Furthermore, he observes that the condition is not recognized clinically until the child is 8 or 9 years old.

In regard to longevity, Clark, Hadley and Chaplin [3] found that few of these patients live beyond 40, but that there are definitely established cases in which the disease has been known to exist upward of fifty years. Some patients contract tuberculosis and develop fibrotubercular diseases; others die of pneumonia or bronchopneumonia.

INCIDENCE

A review of the work of Atkinson [1] and of that of Clark, Hadley and Chaplin [3] yields sufficient evidence in favor of the early occurrence of nontuberculous fibrosis. This is in sharp contrast to the tuberculous variety of the disease.

Atkinson [1] studied a total of eighteen children. The diagnosis of fibrosis was made by clinical signs and roentgenographic studies. Of this number, she found nontuberculous fibrosis in ten cases, while eight were tuberculous.

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2. Herbert, G. T.: Pulmonary Fibrosis, Lancet, 1918, p. 765; Basal Fibrosis in Children, Lancet **1**:1145, 1922.

3. Clark, Hadley and Chaplin: Fibroid Diseases of the Lung and Pleura, 1891.

In a study of forty-five hospital records of pure fibroid disease of the lung, Clark, Hadley and Chaplin [3] found thirty-eight cases in which the age varied between 1 and 30 years, and only seven which varied between the ages of 30 and 65. Of the thirty-eight cases, twenty-two occurred between 5 and 15 years. Tuberculosis was excluded by repeated examinations of the sputum.

SYMPTOMATOLOGY

The cardinal symptoms and signs are (1) recurrent cough; (2) hemoptysis; (3) dyspnea; (4) impaired resonance of one or both apexes or bases of the lung; (5) asthmatoid wheeze, and (6) large crepitant râles.

1. Cough is always present; it is usually productive and is worse at night. It is never spasmodic, as observed in whooping cough. The cough of nontuberculous fibrosis is characterized not only by its persistence over a period of years, but also by the fact that it becomes better and worse from time to time.

Not unlike the history usually elicited in tuberculous children, "catching cold" easily is part of the condition. Any superimposed infection that involves the respiratory organs, e. g., rhinitis or sinusitis, brings the obscure cough into play. The sputum is white and tenacious, but is not the greenish yellow sputum found in tuberculosis. On microscopic examination, various pneumococci and streptococci are found. Repeated analysis of the sputum fails to reveal tubercle bacilli.

2. Large hemorrhagic episodes seldom occur. The tendency of children, as well as of parents, to exaggerate the small quantities of blood spit up should be remembered. Seldom are more than a few drams of blood expectorated. More often the mucoid sputum has streaks of blood coursing through it.

It is generally accepted that hemoptysis is caused by the abrasion of the vessel walls by secondary invading organisms. There is no definite period in the course of the disease during which hemoptysis is known to occur. More often the spitting of blood is encountered long before organization has advanced, although in the later stages hemoptysis is not unknown.

3. Dyspnea is not commensurate to the amount of pathologic change found. It is pronounced after exertion and yet, despite the "air hunger," children enjoy the most strenuous exercises, such as baseball, calisthenics, jumping and running.

4. Pain in the chest is inconstant and is of short duration when it occurs. It is, in all probability, induced by congestion and is usually referred to the anterior aspect of the wall of the chest.

5. Night sweats are generalized and irregular and are not as profuse as in phthisis.

6. In regard to stationary weight or irregular gain, the marked emaciation observed in Koch's disease is not present. When loss of weight occurs, it amounts to a few pounds at the most over many months. Stationary weight is more commonly seen.

7. Two of the sharp points of contrast between tuberculous and nontuberculous fibrosis of the lungs are the normal temperature and pulse rate recorded in the latter.

SIGNS

1. *Appearance of Chest.*—Contraction or flattening of the chest is frequently seen. The right and left sided scoliosis present is dependent on the preponderance of scar tissue in one or the other of the lungs. Expansion is poor and is either equal or unequal.

2. *Displacement of the Mediastinal Organs.*—Contraction of lung tissue caused by fibrosis results in displacement of the heart and trachea. The apex beat is usually displaced a considerable distance within or without the left mammary line. This distortion of the thoracic organs is well demonstrated by roentgenographic studies.

3. *Percussion.*—There is distinct impairment of pulmonary resonance over one or both sides of the chest, usually the lower two-thirds. The degree of impairment will depend on the duration of the disease. Usually the apexes are exempt.

4. *Auscultation.*—The breathing is of the typical puerile (bronchovesicular) or bronchial type. It is impressive to note the large number of râles heard when examining these chests for the first time. Such chests have been reported as the "noisest" types heard. Not uncommonly, the impression conveyed to the examiner by auscultating the chests of such children is that the infection is an acutely spreading one; yet against this assumption are the facts that the thermometer fails to reveal evidence of elevation of temperature and the apparent state of well being displayed by the patient. Pleural friction rubs are most frequent. At times, typical asthmatic breathing is heard and several mistaken diagnoses of bronchial asthma have been recorded. In contrast to the picture of true asthmatic bronchitis is that in the former the asthmatic wheeze is restricted to only one portion of the lung. It further differs from asthma in that no spasmodic attacks occur; the patients are fairly comfortable and enjoy good health.

McNeill [4] suggests that the asthmatic wheeze is due to bronchial spasm or to partial closure of some of the bronchial tubes.

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4. McNeill, C.: Fibrosis of Bronchi and Lung in Childhood following Broncho Pneumonia, Tr. Medico-Chir. Soc. Edinburgh, 1924-25, in Edinburgh Medical Annual, July, 1925.

ROENTGENOGRAPHIC STUDIES

The changes found in the lungs are characteristic. Peribronchial thickening, extending toward the base of the lung with strands of scar tissue in one or both bases, is present. Displacement of the heart and trachea is the rule.

DIFFERENTIAL DIAGNOSIS

Diagnosis by exclusion is the method of choice. Tuberculous fibrosis of the lung is most often confused. Favorable to the diagnosis of the latter are the chronic cough, hemoptysis, night sweats, impairment of resonance of the lungs and râles. The cough in nontuberculous fibrosis is greater at night. The latter condition is further differentiated by the absence of progressive and marked emaciation, negative tuberculin reaction and failure to discover the tubercle bacillus in repeated examinations of the sputum. So important is the last mentioned laboratory observation that it may be safely stated that when repeated examination of the sputum fails to reveal tubercle bacilli, Koch's disease may be dismissed as an etiologic factor. It should be remembered that the true pulmonary type of tuberculosis resembling that of adult life is seldom encountered under puberty. In nontuberculous fibrosis, there is practically always a previous history of infection of the respiratory tract. The temperature and pulse rate are normal or below normal in the nontuberculous type of disease. On the other hand, Koch's disease is characterized by a rapid pulse rate and at some time in the course of the infection by a rise in temperature. Asthenia is slight or lacking, and despite the marked pathologic change, the disability is insignificant when compared with that of the child affected with tuberculosis. The site of the lesions in nontuberculous fibrosis is usually, though not invariably, at the base of the lung. In Koch's disease, the apexes and then the base of the lungs are involved. The Viennese pediatricians rule out the existence of a tuberculous infection on the mere presence of a negative Pirquet reaction. A negative tuberculin reaction, whether dermal or intradermal, in a young child should certainly cause the pediatrician to turn his thoughts to other lesions than those caused by the tubercle bacillus. Recourse to roentgenographic study must be made in ruling out an unresolved pneumonia. A maximum amount of clearing is seen from one year to sixteen months after the onset of the latter condition.

The diagnosis of syphilitic fibrosis must depend on the Wassermann reaction and the roentgen-ray report.

Bronchiectasis is differentiated from the condition by the absence of clubbing of the fingers and toes and also by roentgenographic study.

Foreign body is excluded if there is no history of the patient's having swallowed material alien to the respiratory tract. This information is not always obtained by interrogating the parents. During the "floor"

days of infancy, foreign matter is carelessly introduced into the mouths of the young and often without the parents being aware of what has happened. Roentgenographic study and bronchoscopy must be employed to discover the presence of extraneous substances.

Pneumonokoniosis is practically never seen during childhood. Corroborative facts should be based on a careful history of exposure to the inhalation of dust. The disproportion of dyspnea in children with pneumonokoniosis as compared with that found among individuals in good health is suggestive, although proof of the existing condition must also be determined by a roentgenogram. The roentgenogram will reveal a fine peppering of both lungs with organic particles.

The diagnosis of fungus growths will depend on the discovery of the typical organism in specimens of fresh sputum (*Streptothrix*, *Actinomyces* and *Sporotrichosis*).

TREATMENT

Treatment is purely palliative. Miller [5] advises a dry climate and removal of all infections of the nasal sinuses. For the patients who have developed bronchiectasis, he suggests drainage by inverted posture.

Pierson [6] recommends radical measures. He states that within six months of the onset in early cases and before extensive fibrosis has developed, the patients should have the benefit of artificial pneumothorax. He goes a step further in recommending thoracoplasty in those who show rapid progressions of fibrosis and who have large bronchiectatic cavities. Jacobi [7] speaks highly of the value of the iodides in early cases in which hyperplasia has not gone on to cirrhosis. The treatment with iodides, he states, must be continued over a long period of time. Opiates should be avoided because of the chronicity of the infection and also because they engender disturbed digestion and appetite.

When expectoration is deficient, citrate of soda alone or in combination with small doses of ammonium chloride may be tried.

The turpentine derivatives (creosote, guaiacol and terebene) have been sad disappointments in the hands of most pediatricians.

Tonic treatment with syrup of ferrous iodide, Fowler's solution, the simple bitters and cod liver oil is justifiable. These should be given a thorough trial before being discarded. An abundance of sunlight and fresh air is imperative at all times.

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5. Miller, J. A.: Nontuberculous Pulmonary Infections, Am. J. M. Sc. **54**:805, 1917.

6. Pierson, P. H.: Post Influenzal Lung Conditions, M. Clin. N. Amer. **6**:1509, 1923.

7. Jacobi, A.: Peribronchitis and Interstitial Pneumonia, Am. J. M. Sc. **20**:1, 1903.

REPORT OF CASE

History.—A white boy, aged 7 years, was first seen, May 8, 1923. The chief complaint was the spitting of blood and cough. The family history was negative. The boy had walked and talked at the age of 22 months. He had had a summer complaint at 6 months, rickets at 10 months, and two attacks of bronchopneumonia at 7 months and 6½ years, respectively. The second attack of pneumonia was relatively severe. He had had measles and whooping cough at the age of 2 years, followed by chickenpox. There was no history of exposure to tuberculosis or of the swallowing of a foreign body. He had had repeated colds since the age of 10 months, usually in winter.

A severe cold in 1916, when he was 6 months old, was diagnosed as bronchial asthma by the family physician. He had had many similar colds since that time. Such colds were accompanied by a great deal of coughing and expectoration of grayish yellow mucus. The attacks lasted, as a rule, for one or two weeks. During the winter of 1925 and 1926, the patient was in fairly good health, and did not experience the customary colds. The mother stated that he had always been underweight.

Until two or three years previously, the child did not play like other children but displayed a listless, inert manner. During the following two or three years he was active and played vigorously. He attended an open air class in 1924, and a nutrition class at public school.

The present illness began early in November, 1926, when he developed a sore throat and cough, and spit up from one to two tablespoonfuls of bright red blood. Improvement followed medical care, and the boy returned to school. On Dec. 11, 1926, he again coughed up some blood. The last hemorrhagic episode was followed by the expectoration of blood-streaked sputum for one week.

Physical Examination.—The first examination was made on May 8, 1923. The boy was emaciated and poorly nourished. Pallor of all the mucous membranes was present. The chest was long, narrow and flat; the supraclavicular fossae were prominent, especially on the left side, and there was a flattening below the clavicle on the left side. Expansion was poor throughout the entire chest, especially on the left side. Vocal fremitus was strong over the upper lobes. Percussion of the right lung showed: impaired resonance of the upper lobe to the second rib anteriorly and resonance below the second rib; impaired resonance of the upper lobe posteriorly to the level of the fourth vertebra and hyperresonance below; hyperresonance of the axilla. The left lung showed: impaired resonance anteriorly to the second rib and posteriorly to the fourth dorsal vertebra. Auscultation of the right lung showed: breath sounds well heard throughout, loudest in the lower lobe posteriorly. Expiration was prolonged throughout (bronchovasicular type). There were a few fine râles in the sixth interspace, midaxilla. Occasional fine râles were scattered posteriorly. Whispered voice sounds were not heard. The left lung showed: breath sounds almost inaudible during quiet breathing; on deep breathing, distant tubular breath sounds in small areas anteriorly and posteriorly; many large moist râles throughout. Rough friction sounds were heard throughout the left side. The heart did not show any shock or thrill. The apex beat was heard in the fifth interspace of the midline. The sounds were well heard, with good tones and no murmurs.

Subsequent examinations, at intervals of about one year, showed physical characteristics similar to those found on the first examination, with slight extension downward of the pathologic process in both lungs.

Fig. 1.—Excessive amount of fibrosis and peribronchial thickening of the entire right lung and the upper lobe of the left lung.

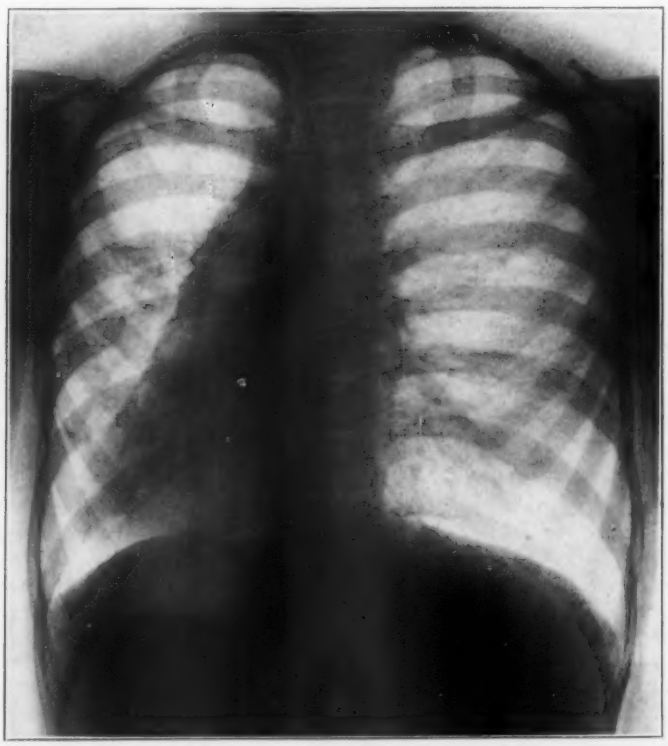

Fig. 2.—Irregular strands in the right and left lung fields. The large shadow of the heart is drawn into the left lung by the scarring process.

Clinical Tests.—1. Examinations of the Sputum: Eleven examinations were made at various intervals from May 12, 1923, to Dec. 31, 1926. No tubercle bacilli were found; the sputum was negative for mycosis organisms. The blood gave a positive reaction on several examinations. Pus cells and a few diplococci were present.

2. Inoculation of Sputum Into Guinea-Pig: After inoculation on Jan. 8, 1927, by the antiformin method, the guinea-pig did not develop any symptoms of disease. The animal was killed at the end of six weeks; gross and microscopic examinations for tuberculosis were negative.

3. Examination of the Feces for Tuberculosis: On April 25, 1927, the examination was negative.

4. Examination of the blood showed: The Wassermann reaction on Dec. 20, 1926, was negative. The blood count was: hemoglobin, 75 per cent; red blood

Data of Course of Nontuberculous Fibrosis

Date	Temperature *	Pulse	Respiration	Weight
5/ 8/23	98.1	100	32	37½ pounds
5/19/23	98.2	112	26	39 pounds
5/26/23	98.3	100	24	38 pounds
6/ 2/23	97.4	90	30	36½ pounds
6/ 9/23	98.2	100	26	37 pounds
6/16/23	98.0	88	20	37½ pounds
5/30/23	98.0	94	22	37½ pounds
9/29/23	99.0	112	34	38 pounds
10/13/23	97.1	88	24	40 pounds
10/20/23	96.2	88	28	39½ pounds
10/27/23	97.4	88	22	40 pounds 2½ oz.
1/10/24	97.4	88	24	40 pounds
3/ 1/24	98.0	100	28	44 pounds
3/15/24	98.0	100	28	42 pounds
3/20/24	97.0	98	28	43½ pounds
4/12/24	97.0	98	24	42½ pounds
4/ 2/24	97.0	90	28	43 pounds
5/ 8/24	98.0	100	28	46 pounds
5/12/24	98.0	90	28	46 pounds
5/19/24	98.2	108	40	43¾ pounds
6/ 5/24	97.4	100	22	43½ pounds
12/20/26	98.0	88	26	51 pounds
12/21/26	98.6	94	28	51 pounds
12/22/26	98.8	88	30	52¼ pounds
4/30/27	98.3	82	40	52 pounds

* The temperature recorded was the highest elevation observed (by mouth) between the hours of 8 a. m. and 8 p. m.

cells, 4,450,000; white blood cells, 8,000; color index, 0.9; polymorphonuclears, 30 per cent; small mononuclears, 60 per cent; large mononuclears, 40 per cent; eosinophils, 1 per cent; transitionals, 5 per cent.

5. Urinanalysis: Seven examinations were negative for tuberculosis, sugar, albumin, or casts.

6. Tuberculin Tests: The Pirquet test was negative. Mantoux tests made with 0.1 mg. and 0.01 mg. of Koch's old tuberculin (human) were negative.

7. Roentgenographic Studies: Five studies were made at intervals of about one year. The right lung showed irregular strands as low as the anterior level of the third inner space. The left lung showed similar strands throughout the lung field. Many were massed together at the anterior level of the third rib. The appearances were not typical of tuberculosis. The lesion did not resemble bronchiectasis. The cardiac shadow was large. The heart was slightly drawn into the left lung field, apparently by a scarring process. A roentgenologist of unusual ability and experience had never seen tuberculous scarring produce such marked displacement of the heart.

COMMENT

When the boy was first seen, a mistaken diagnosis of pulmonary tuberculosis was made. The erroneous conclusion was based on chronic cough and physical signs in the chest not unlike those of Koch's disease. The negative Pirquet reaction was assumed to be part of a severe infection that depleted the system of antibodies. The absence of tubercle bacilli by repeated examinations of the sputum and the comparatively normal temperature and pulse rate led to a suspicion of nontuberculous infection of the chest. The final points in favor of the latter condition have already been summed up under the differential diagnosis.

The case is of interest, as the asthmatic wheezing observed on several occasions was not limited to any one part of the lung, but was diffuse. The paroxysmal attacks common in the true asthmatic patient were absent and the dyspnea slight.

A second point of importance in the case is that the apexes as well as the bases of both lungs shared in the pathologic process. The latter observations were determined by physical examination and roentgenograms.

CONCLUSION

1. A case of nontuberculous fibrosis of the lungs is presented in a boy of 11.

2. The diagnosis of this condition is often confused with the true pulmonary form of tuberculosis seen in the adult, because of allied symptoms and signs common to both diseases.

3. Conclusive evidence of the existence of fibrosis of nontuberculous origin is based on a history of bronchopneumonia, hemoptysis, impaired pulmonary resonance accompanied by large râles ("noisest chest," so called), and repeated negative examinations of the sputum.

4. Despite the pathologic change in the chest, the disease is not necessarily fatal, nor does it seriously interfere with a vital and useful life.

1426 Spruce Street.

ISOLATED LYMPHOID HYPERPLASIA IN THE CECUM AND APPENDIX OF CHILDREN*

A. P. STOUT, M.D.
NEW YORK

During the past few years, a lesion has come to my notice which affects portions of the gastro-intestinal tract in children and which has apparently been neglected by medical authors to such an extent that it is not at all well known. This lesion is an isolated or localized hyperplasia of lymphoid tissue in the cecum and appendix without a condition of status lymphaticus, or, so far as one can tell without necropsy, of hyperplasia of the lymphoid tissue of other parts of the intestinal tract. The condition has clinical significance, because in two of the three cases I will report, the tumor-like growth of lymphoid tissue initiated processes that required immediate surgical intervention. In one instance a tumor-like mass in the ileocecal valve caused an intussusception; in the other, the appendix was obstructed where it joined the cecum, and the dilated distal portion was acutely inflamed and filled with pus when it was removed. The third case involved the tip of the appendix alone and apparently was not responsible for any symptoms.

When seen grossly, the lymphoid tissue makes an isolated nodule which can be seen easily and which feels soft. When it is cut into, it is found to lie in the submucosa. In one of the cases in which the appendix was involved, it pushed the mucosa into the lumen until the opposing sides met and then expanded peripherally, bowing out the muscular and serous coats to form an externally visible fusiform swelling. In the other there was no lumen or mucosa, and the distal half of the appendix was solidly filled with lymphoid tissue. That the tension is considerable may be judged from finding lymphoid tissue forced through one of the defects in the mesenteric border of the muscular coat through which the blood vessels reach the submucosa. In the case of the ileocecal valve, there is plenty of room for expansion into the lumen of the cecum, so that no tumor is seen externally but the mass can be palpated through the cecal wall, and when the mucous surface is inspected the swelling appears nodular, like a papillary adenoma. When cut, the lymphoid tissue bulges forward and is a pale cream, with a tinge of yellow. Microscopically, one finds merely congeries of large so-called "germinal centers" surrounded by masses of

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* From the Laboratory of Surgical Pathology, Presbyterian Hospital, New York.

lymphocytes. Some of the cells in the germinal centers show mitosis, while others have only fragments of nuclear material in them. Otherwise, there is nothing unusual about them except their increased number and possibly their large size.

It is common knowledge that lymphoid tissue is peculiarly rich in the gastro-intestinal tract of children at birth and that gradually it grows less in amount as they grow older. Perrin and Lindsay [1] have pointed out that it is due probably to the great amount of lymphoid tissue normally present in the ileocecal valve, in children under 1 year, which makes ileocecal intussusception the commonest form during this period, while, after one year, the amount of lymphoid tissue here grows less but increases in the terminal ileum, so that ileocolic intussusception is more common in older children. Perrin and Lindsay feel that the unusual swelling is due to edema of a Peyer's patch or other lymphoid tissue incidental to gastro-enteritis. As far as one can tell, they seem to think it is part of a generalized process and not a localized lymphoid hyperplasia.

A moderate degree of hyperplasia involving all the lymphoid tissue of the appendix in children and accompanied by symptoms resembling acute appendicitis was first described by Barss [2] and later by Symmers and Greenberg [3] and Smith.[4] The only basis for this association seems to be that nothing could be found in these appendixes except a rich layer of lymphoid tissue in the submucosa, and that following removal of the appendix the children were relieved of symptoms. We also have observed similar cases but have hesitated to incriminate the lymphoid tissue because the considerable average variation of lymphoid tissue in children makes it difficult to judge where the normal ends and hyperplasia begins. Symmers has suggested that these are local manifestations of status lymphaticus. His reason for so thinking is the finding of evidences of degeneration and necrosis in the germinal centers, which he says he has observed only in status lymphaticus. This seems to us to be an insufficient basis for such a suggestion because, as Latta [5] has demonstrated, even in embryonic life the germinal center is probably not only a focus for the production of cells, but an area

1. Perrin, W. S., and Lindsay, E. C.: Intussusception. A Monograph Based on Four Hundred Cases, Brit. J. Surg. **9**:46, 1921.

2. Barss, H. deB.: Lymphatic Disease in Children Simulating Appendicitis, Am. J. Dis. Child. **15**:421 (June) 1918.

3. Symmers, D., and Greenberg, M.: The Clinical Significance of Lymphoid Hyperplasia of the Appendix, J. A. M. A. **72**:468 (Feb. 15) 1919.

4. Smith, T. A.: Lymphoid Hyperplasia of Appendix in Children, Ann. Surg. **79**:871, 1924.

5. Latta, J. S.: The Histiogenesis of Dense Lymphatic Tissue of the Intestine, Am. J. Anat. **29**:159, 1921.

of degeneration with phagocytosis of nuclear remnants, and Heilmann [6] has noted similar phenomena in the germinal centers of inflamed appendixes in adults. However, Heilmann thinks that appendical symptoms in adults may be explained on the basis of changes in the lymphoid tissue. In any event the lesion is different from the one I am describing.

Such disturbances of the lymphoid apparatus as nodular enteritis with and without ulceration, glandular fever, typhoid fever, generalized giant lymph follicle hyperplasia of lymph nodes and spleen [7] and other similar lesions may be dismissed without further discussion as being generalized rather than localized lesions.

In 1910, Wilhelm and Delval [8] described and pictured a sessile tumor the size of a pea, which projected into the lumen near the tip of the appendix of a boy, aged 17. This was made up of lymphoid tissue and is the first case of localized lymphoid hyperplasia of which I can find mention. It differs from my cases in that it is not in a young child and does not involve the entire circumference of the organ; nevertheless, it belongs to the same class of lesion.

Lehmann [9] reported a similar case in the tip of the appendix of a girl, aged 20, and in addition two other cases in which the rectum [10] was the site of the lesion and the masses were removed under the misapprehension that they were adenomatous polyps. One case occurred in a woman, aged 45, who had a mass the size of a hazelnut near the anus; in the other case, a man, aged 35, had two sessile tumors of lymphoid tissue the size of a pea removed from his rectal wall 7 cm. from the anus. Lehmann refers to two other cases of small tumors

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6. Heilmann, P.: Ueber Veränderungen des lymphatischen Gewebes im Wurmfortsatz und im Allgemeinen, Virchows Arch. f. path. Anat. **258**:52, 1925.

7. Brill, N. E.; Baehr, George, and Rosenthal, N.: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen, J. A. M. A. **84**:668 (Feb. 28) 1925.

8. Wilhelm, A., and Delval, C.: Tumeur inflammatoire de l'appendice, Bull. et mém. Soc. anat. de Paris **85**:771, 1910.

9. Lehmann, H.: Unter dem Bilde der "Polyposis" in Erscheinung tretende, umschriebene Hyperplasia des lymphatischen Gewebes im Dickdarm, Deutsche Ztschr. f. Chir. **190**:391, 1925.

10. Since this paper was prepared, a similar case has been found in the rectum of a 7 year old girl. She had suffered for two weeks with tenesmus, and her mother noticed a lump. At operation a pedunculated polyp 1 cm. in diameter was removed from a point 5 cm. from the mucocutaneous junction. It was covered with mucous membrane and was made up entirely of a mass of lymphoid tissue in the submucosa. One year after operation she was well except for a tendency to constipation. A similar case was also found in which the lesion was mistaken for a polyp in the rectum of a man, aged 44, and a comparable isolated mass of lymphoid tissue was observed in the skin of the cheek of a woman, aged 58. This was 1 cm. in diameter and was mistaken for a fibroma.

of the appendix which he thought were probably similar, but as no microscopic examination was made, it does not seem justifiable to include them.

With the exception of these four cases reported by Wilhelm and Delval and Lehmann, I can find no other mention of this lesion.

REPORT OF CASES

CASE 1.—*History.*—D. H., a boy, aged 5 months, at 2 months had awakened one morning pale, crying, with knees drawn up, evidently suffering from abdominal cramps. He vomited several times and was treated with external heat and two enemas, one of which returned blood-stained. Two and a half hours after the onset, the attacks ceased. At this time, the blood count was white blood cells, 14,800; polymorphonuclears, 59 per cent; small lymphocytes, 25 per cent; large lymphocytes, 14 per cent; transitionals, 1 per cent. There was no further trouble

Fig. 1 (case 1).—The thick terminal ileum, the constriction at the ileocecal junction, the appendix and above the cecum and ascending colon.

until the morning of admission three months later when he again had abdominal cramps, vomiting and the passage of a small amount of blood and mucus. Two enemas failed to relieve him, and he was brought to the hospital. Examination of the abdomen showed a rigid lower right rectus muscle, but no mass was felt. There was little distention, but a roentgenogram made after a barium enema showed an obstruction at the splenic flexure.

A diagnosis of intussusception was made.

Operation was performed, May 19, 1924, by Dr. John M. Hanford. An intussusception was found extending from the ileocecal region to the middle of the transverse colon. It included the appendix and was easily reduced by manipulation. After reduction the operator noted a movable mass at the ileocecal junction, which apparently could be passed back and forth between ileum and cecum. With the idea that it was a polyp that might be excised, the cecum was opened. Inspection showed that the mass felt was a projection of the ileocecal valve into the cecum. Fearing a recurrence of the intussusception, the operator decided on resection to prevent this and removed the terminal ileum, cecum and appendix with end-to-end anastomosis of ileum to colon.

Result.—During convalescence, the child had to have an ear opened, and a hernia developed in the scar. He had some peribronchial infiltration, as shown by roentgenograms of the chest, but this cleared up. The case was followed for thirty-five months and he was developing normally. No enlargement of the thymus, spleen or lymph nodes had been noted.

Pathologic Examination.—The specimen included 6 cm. of the terminal ileum, 4 cm. of cecum and ascending colon and an appendix 5 cm. long and 4 mm. thick. Just proximal to the ileocecal valve the ileum was thickened and dusky, measuring 2 cm. in diameter, whereas proximal to this it was only 1.2 cm. in diameter. There seemed to be a definite constriction at the junction itself. The appendix also had congested vessels. On opening the colon and inspecting the ileocecal region, one saw a rounded nodular tumor, 1.7 cm. in diameter, which was soft and covered with mucous membrane. On longitudinal section one found that the tumor was really a greatly swollen ileocecal valve and that the swelling was due to an

Fig. 2 (case 1).—Appearance of the colon after it had been split open and reflected to show the nodular mass formed by the thickened ileocecal valve which was responsible for the intussusception.

accumulation of soft, pale tissue beneath the mucosa. The same type of tissue could be seen in the submucosa of the terminal ileum and was responsible for its increase in diameter.

Microscopic examination showed that all of the increase in size noted was due to large groups of germinal centers surrounded by masses of lymphoid cells. Among the nuclei of the germinal center cells, there were a number that showed pyknosis and others that showed mitosis. Many reticulum cells showed vacuolization of cytoplasm. The mucosa and muscularis were intact. In the mesenteric fat were small patches of lymphoid cells and some lymphatics which were dilated and contained lymphoid cells. A mesenteric lymph node was about 4 mm. in diameter and did not show any lymphoid hyperplasia but did show wide dilatation of the sinuses and hyperplasia of the reticulum, and in its meshes could be seen lymph, red blood cells, lymphocytes and other wandering cells. There was lymphoid tissue in the submucosa of all parts of the gastro-intestinal tract removed, but it varied greatly in amount.

CASE 2.—*History.*—J. L., a girl, aged 8½ years, had had measles and whooping cough, and her tonsils had been removed at the age of 6. In the morning of the day before admission, she complained of abdominal colicky pain radiating to the right lower quadrant. Several hours after the onset she vomited, was constipated and had urinary frequency, headache and fever. Examination at the hospital showed tenderness in the right lower quadrant but no rigidity. The pharynx was reddened, and there were palpable cervical lymph glands. The heart was slightly enlarged, the second pulmonic sound being greater than the second aortic sound, and there was a questionable systolic murmur. The temperature was 100 F., the pulse rate, 120 and respiration, 24. The white blood cells numbered 16,800, and the polymorphonuclears, 87 per cent. The urine was normal. The operation, performed on Feb. 27, 1927, was supervised by Dr. John M. Hanford. The appendix was reddened, coiled, enlarged, firm, turgid and rigid. It was resected without drainage.

Fig. 3 (case 1).—A longitudinal section with the ileum at the right and the cecum and colon at the left, showing the great accumulation of lymphoid tissue in the terminal ileum and ileocecal valve.

Postoperative Course.—On the third postoperative day, the temperature rose to 105.4. It continued to be high, and a subcutaneous abscess was drained in the upper angle of the wound. On the sixth day, exploration was done, and a subcecal peritoneal abscess was found and drained. There was nothing in the pelvis. Soon the liver enlarged; the patient looked yellow, and on the ninth day bile was found in the urine. Roentgen-ray examination of the chest at this time was negative. Blood culture was sterile, but cultures from the wound showed *Bacillus coli.* Her condition became worse rapidly and she died on the tenth day after appendectomy. Necropsy was not obtained, but it was thought that she died of pylephlebitis.

Pathologic Examination.—The appendix was 6 cm. long and was divided into thirds by two nearly right-angled angulations. The distal two-thirds was a deep, dusky red, and the serosa was dull, although no exudate appeared on its surface. Its diameter varied from 7 to 10 mm. The proximal portion was pale, oat-shaped and firm; the contrast between the two portions at the proximal angulation was

striking. On longitudinal section, one found at the proximal angulation a potential obstruction of the lumen, due apparently to this angulation. Distal to it the lumen was widely dilated, filled with semi-solid bloody débris; the wall was less than 1 mm. thick and the mucous surface ragged and dusky red. Proximal to it, the lumen was only a potential space, because the wall here averaged 4 mm. in thickness, owing to an accumulation of soft, faintly yellow tissue in the submucosa which bulged toward the cut surface when it was cut into.

Microscopic examination of the distal portion showed simply the changes incidental to acute inflammation, i. e., partial destruction of the mucosa, intense

Fig. 4 (case 1).—Section through the ileocecal valve with the muscularis at the right, the mucosa at the left and between the masses of lymph follicles in the submucosa. Below is some of the lymphoid tissue in the submucosa of the cecum for comparison.

polymorphonuclear leukocytic infiltration, vascular engorgement and thrombosis, etc. In the proximal portion the mucosa was intact, and the only evidences of acute inflammation were a certain amount of polymorphonuclear leukocytic infiltration of all the coats. The most striking feature, however, was the presence of a great quantity of lymphoid tissue in the submucosa. This was made up of congeries of germinal centers and small lymphocytes between them. The centers were often irregularly shaped instead of being rounded, and the nuclei of the cells showed both mitoses and pyknosis. Some of the reticulum cells scattered among the small lymphocytes showed vacuolization of the cytoplasm.

CASE 3.—*History.*—M. C., a girl, aged 9 years, presented a long, complicated history in which the appendix may or may not have been a causative or contributory factor. The child's mother was the "worrying" type. The child herself was a bed-wetter. Her complaints were: attacks of pain in the right upper quadrant, which radiated to the right thigh following urination. They were associated with fever and nausea and with urgency and frequency of urination. She was studied for some weeks, and the examination showed: the genito-urinary and gastro-intestinal tracts were normal; the stools were negative for ova, parasites and blood; the urine was always negative for albumin and usually was negative microscopically, but red blood cells were reported once and "pus" once. The white blood cells numbered 9,500; polymorphonuclears, 65 per cent; small lymphocytes, 30 per cent; large lymphocytes, 5 per cent. The Wassermann reaction was negative. Her weight was 67 pounds (30.4 Kg.). The temperature varied from 98.4 to 100.2 F. At times there was tenderness in the right lower quadrant, but this was the only positive physical sign. An exploratory operation was done, March 2, 1923, by Dr. John M. Hanford. The appendix was free and directed upward on the posterolateral aspect of the cecum. The meso-appendix was "fibrosed" so as to

Fig. 5 (case 2).—At the left is the distal portion of the appendix emptied of its contents and showing its inflamed state. At the right is the cecal portion with the masses of lymphoid tissue thickening its submucosa and causing a potential obstruction at its junction with the inflamed portion.

kink the appendix at its middle. The distal half was slightly thickened, congested and indurated. In the ileocecal mesentery were 4 lymph nodes, the largest being about 5 mm. in diameter. A careful exploration of the peritoneal cavity showed nothing further. The spleen felt normal. The appendix and one gland were excised.

Postoperative Course.—The patient was relieved of symptoms for about three months, when she began to have lower abdominal colicky pains, occasional enuresis and nail biting. During the next two and a half years, she was studied exhaustively. Cystoscopy showed some congestion of the bladder mucosa, but a pyelogram of the right kidney was normal. Catheterized urine was negative to all tests, including the injection of guinea-pigs. Roentgenograms of the abdomen were negative for calcified nodes, and a stereoscopic roentgenogram of the chest was negative. Positive symptoms were a slight umbilical hernia, slight enlargement of the isthmus of the thyroid, a basal metabolic rate of — 16 per cent, a pulse rate of 88 and enlargement of the tonsils and cervical lymph nodes. She was given helio-therapy and thyroid extract and had her tonsils removed (at another hospital),

Oct. 15, 1926. During all this time her growth was continuous, and the abdominal pains finally ceased. She was last seen thirty-five months after the appendectomy was performed and at that time was free from symptoms.

Pathologic Examination.—The appendix was 6 cm. long and varied from 6 mm. in diameter in the proximal portion to 1 cm. in the distal portion. The serous surface was smooth, and the surface vessels were engorged in the distal half. At the junction of the proximal and middle thirds, the appendix was angulated. Longitudinal section showed that in the proximal half the wall varied from 2 to 3 mm. in thickness and that the mucosal folds almost met, so that there was little soft débris in the lumen. This was the characteristic appearance of the appendix in a child, aged 9. In the distal half, there was no lumen; the entire space inside the muscular coats was filled with a soft, yellow-tinged, relatively homogeneous mass which bulged outward toward the cut surface. The vascular defects in the mesenteric border of the distal half were broad, one of them more than 1 mm.,

Fig. 6 (case 3).—At the right is the tip of the appendix; the soft mass of lymphoid tissue can be seen filling the entire space inside the muscular walls and ending abruptly near the center of the organ.

and some of the yellowish material seemed to project outward between the muscle coats.

A cross section taken from the distal half showed that the yellowish material inside the muscle coat was an almost solid mass of lymphoid tissue with large germinal centers and masses of small lymphocytes between them. The germinal centers were made up of the usual large cells whose nuclei showed activity in the form of occasional mitoses and regressive changes in the form of occasional pyknosis and nuclear disintegration. With the small lymphocytes, one found connective tissue, capillaries, occasional eosinophilic leukocytes and cells with melanotic pigment, i. e., the usual phenomena of the appendical submucosa. The lymphoid tissue with its germinal centers projected through one of the vascular defects of the muscularis well out into the fat of the mesenteriolum. The muscular and subserous coats showed no recognizable pathologic changes except for the presence of a few dilated lymphatic vessels crowded with lymphocytes—something that has been found in many appendixes of both adults and children.

A section from the proximal half of the appendix showed a generous supply of lymphoid tissue beneath a mucous membrane that was intact. The germinal centers were large and showed both mitoses and destructive changes as they did in the other half. The destructive changes were marked; in one instance, a patch of actual necrosis could be seen. No other definite lesions were recognized.

The mesenteric lymph node that was removed was about 1 cm. in diameter and was soft, encapsulated and homogeneous on cross section. It showed a generalized increase in the lymphoid cells but hardly any germinal centers. There was no hyperplasia of the reticulum cells nor were the sinuses dilated. There was a slight degree of fibrosis in two isolated areas.

PHYSIOLOGIC VARIATIONS IN THE LEUKOCYTES IN INFANTS AND IN CHILDREN *

E. GORDON FLETCHER, M.D.
AND
A. GRAEME MITCHELL, M.D.
CINCINNATI

Considerable study has been carried out on the normal variation in the number of leukocytes in the capillary blood. It is not our intention in this paper to review the subject, and the reader may be referred to a previous article by one of us [1] and to recent articles by Sabin and her co-workers [2] and by Shaw.[3] Briefly summarized, the observations made by different investigators are as follows:

(*a*) In children and adults, digestive leukocytosis is inconstant.

(*b*) A rise in the total leukocyte count occurs in the afternoon and also in the early morning, regardless of the effect of food.

(*c*) Animals such as dogs, cats and rabbits develop a leukocytosis after food rich in protein.

(*d*) Protein food seems to be more constantly productive of leukocytosis than carbohydrate or fat.

(*e*) Several factors influence the number of leukocytes as ordinarily counted in the capillary blood. Among these should be enumerated increased muscular activity (crying, struggling and exercise), changes in the blood pressure, changes in the temperature of the body, changes in posture, increased nervous excitability and the like. It is only necessary to mention in this connection the various pathologic conditions that affect the leukocyte count.

(*f*) The careful studies of Sabin and her co-workers show that there is a characteristic rhythm of the total number of leukocytes with an interval of approximately an hour's duration. The total number of leukocytes may vary as much as 100 per cent in the course of several hours and the individual varieties of leukocytes as much as 100 or 200 per cent.

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* From the B. K. Rachford Department of Pediatrics, College of Medicine, University of Cincinnati and the Children's Hospital.

* Read at the Pediatric Seminar, University of Cincinnati, March, 1927.

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2. Sabin, F. R.; Cunningham, R. S.; Doan, C. H., and Kindwall, J. A.: Bull. Johns Hopkins Hosp. **37**:14, 1925.

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We have been unable to find any previous observations in which the leukocytes were studied in infants and children over the entire twenty-four hour period. The investigation of Shaw, published after our paper had been completed, was on adults, in four of whom the twenty-four hour fluctuation in leukocytes was noted. The work that we are reporting was carried out on four normal infants between the ages of 1 and 3 months and on four children whose ages were 3, 6, 11 and 13 years, respectively. In patient 1, the mononuclear cells were

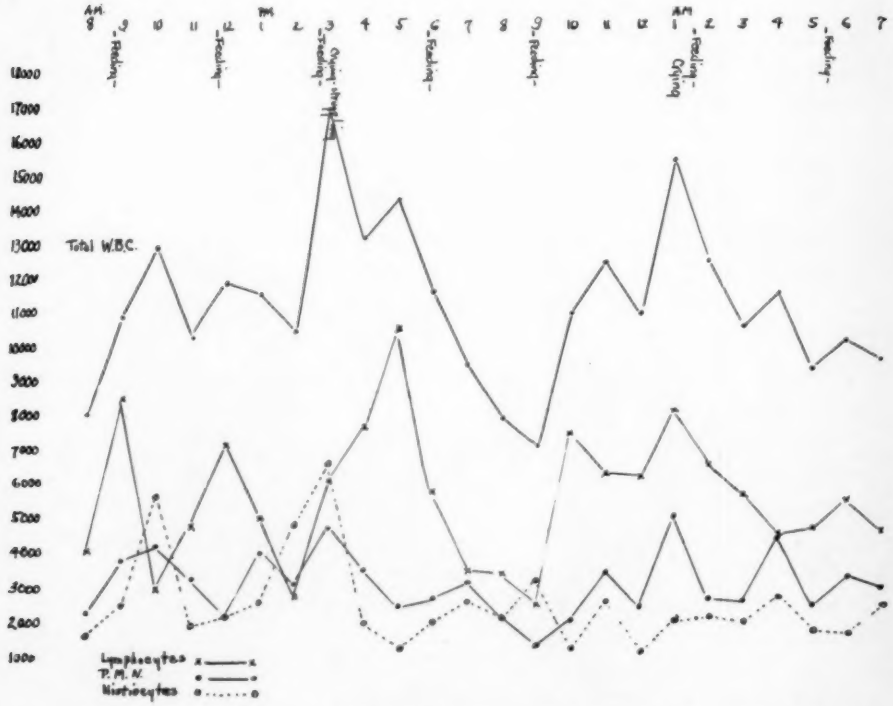

Chart 1.—Variations in leukocyte count in infant, aged 6 weeks, fed on Protein S M A.

classified as histiocytes. The total and differential counts were made every hour. The exact time of feeding was noted and also the occurrence of any factor such as crying, struggling or the like which might influence the count. The same pipet and counting chamber were employed during a series, and all precautions were used to make the technic as uniform as possible.

Analysis of the results that are presented in detail in the charts reveals the following:

Seven of the eight patients showed a rise in the total leukocyte count in the early afternoon (from 2 to 4 p. m.).

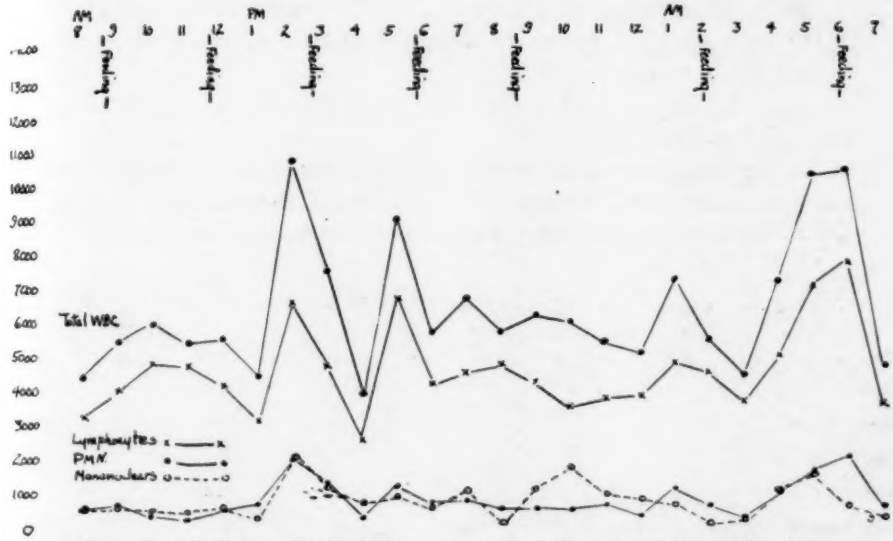

Chart 2.—Variations in leukocyte count in infant, aged 3 months, fed on breast milk.

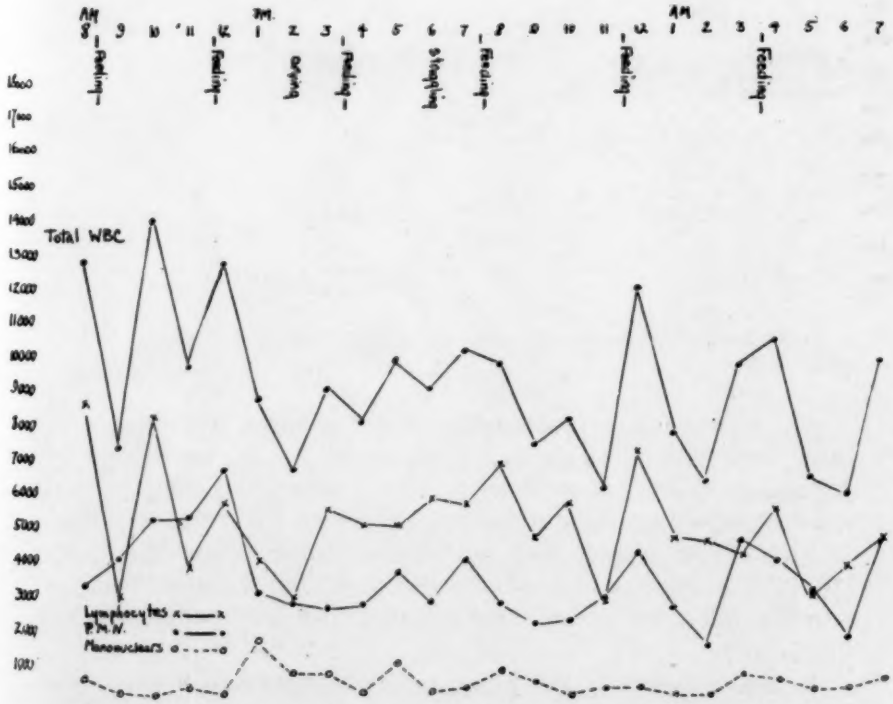

Chart 3.—Variations in leukocyte count in infant, aged 2 months, fed on breast milk.

All of the eight patients showed a rise in the total leukocyte count in the early morning (from 12 midnight to 1 a. m. in six cases and from 3 to 4 a. m. in two cases).

Seven of the patients showed a fall in the total leukocyte count between 7 and 8 a. m.

In the late evening, all of the patients showed a fall in the total leukocyte count. In seven cases, this occurred between 7 and 10 p. m., and in the other the fall did not begin until after 10 p. m.

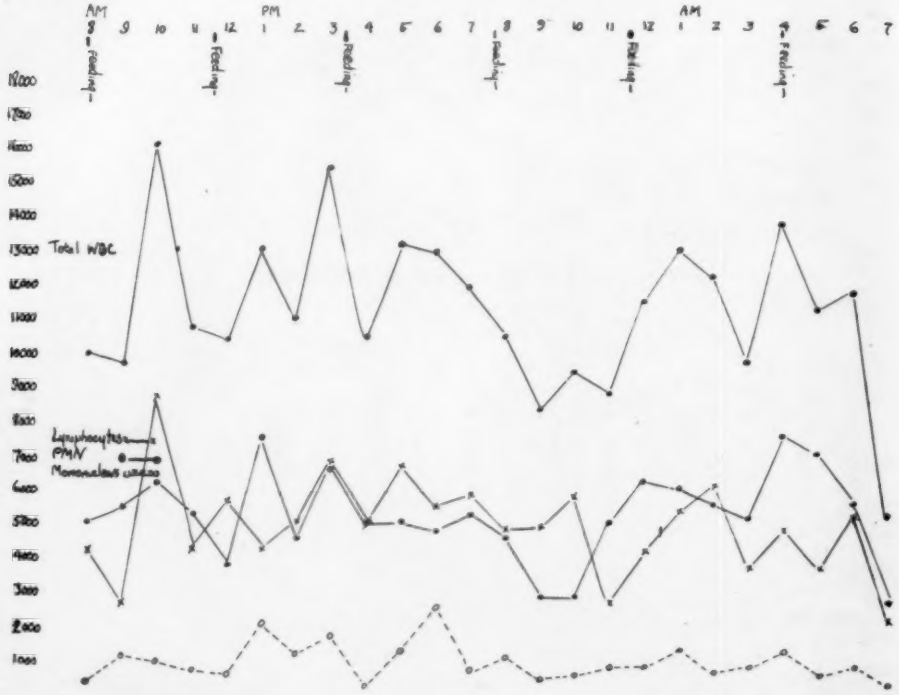

Chart 4.—Variations in leukocyte count in infant, aged 1 month, fed on breast milk.

The highest leukocyte counts in the day occurred at the following times: two at 10 a. m., one at 2 p. m., one at 3 p. m., two at 4 p. m., one at 7 p. m. and one at 10 p. m.; that is, four of the eight patients had their highest counts in the afternoon between 2 and 4 p. m.

Five of the patients had their lowest leukocyte counts between 5 and 7 a. m.; one at 10 a. m.; one at 3 p. m., and one at 9 p. m., but even the last three patients had comparatively low counts between 5 and 7 a. m.

In the four infants the leukocyte counts were not constant, but there was a tendency to a decrease in the leukocytes after feeding,

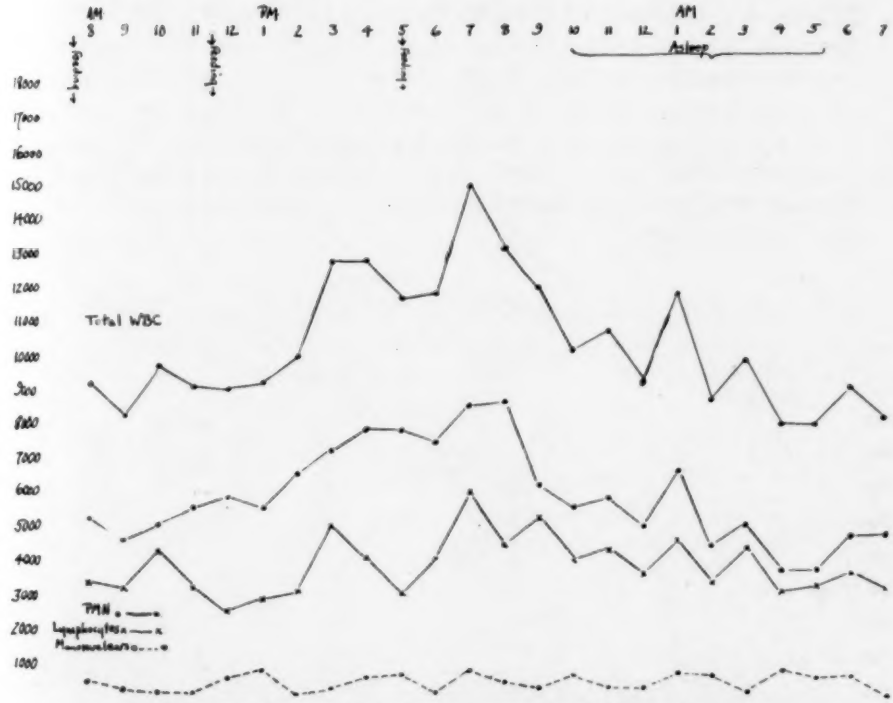

Chart 5.—Variations in leukocyte count in child, aged 6 years.

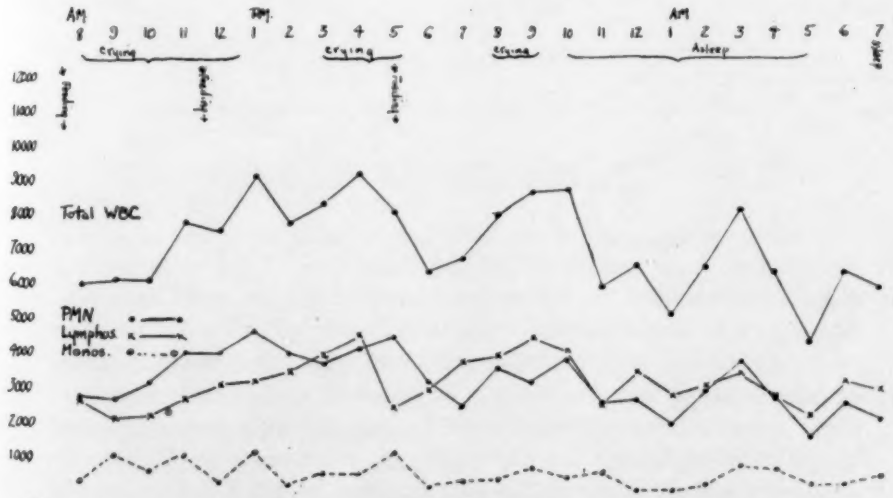

Chart 6.—Variations in leukocyte count in child, aged 3 years.

fifteen (57.7 per cent) of the feedings being followed by a fall in the leukocyte count and ten (38.5 per cent) by an increase; in one there was no appreciable change. In the four older children who were fed three times a day, there was a rise after nine meals (75 per cent), a fall after two meals (16.6 per cent) and no change after one meal. A previous study already cited, of fifty infants, in which half hour intervals were employed, showed a decrease in the count after 68.5 per cent of the feedings.

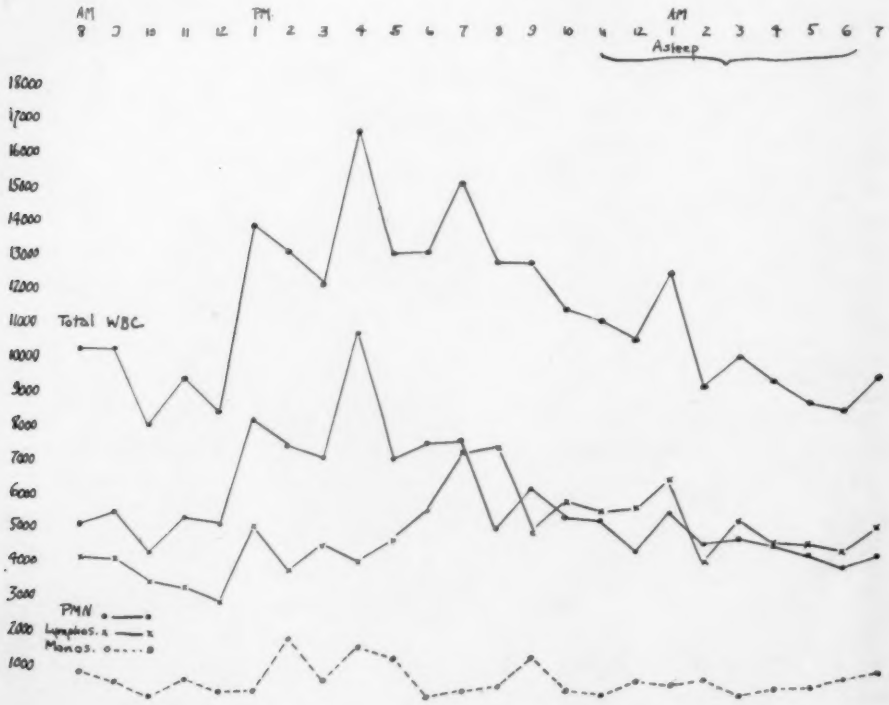

Chart 7.—Variations in leukocyte count in child, aged 11 years.

This series is too small to enable one to draw any conclusion as to the relation of the feeding at any particular time of day to increase or decrease of the cells. In the previous study of fifty cases, no such relationship could be established.

In accordance with the observations of Sabin and her co-workers in adults, there was usually an increase in the polymorphonuclear count corresponding to the time of increase of total leukocyte count in the older children. In the young infants, however, it was the lymphocytes that closely followed the curve of total leukocytes, the polymorphonuclears also tending to fluctuate with the total leukocytes but to a lesser degree.

The variations in the total leukocyte count were large, especially in the infants. The increase was at times as much as 175 per cent; that is, the highest count was that much greater than the lowest.

During the twenty-four hours, the polymorphonuclears varied as much as almost four times their number; that is, the highest count was as much as four times the lowest.

During the twenty-four hours the lymphocytes varied as much as two and a half times their number; that is, the highest count was two and a half times the lowest.

The large mononuclear cells varied considerably during the course of the day, although their number was seldom such as to affect the total count to any marked degree.

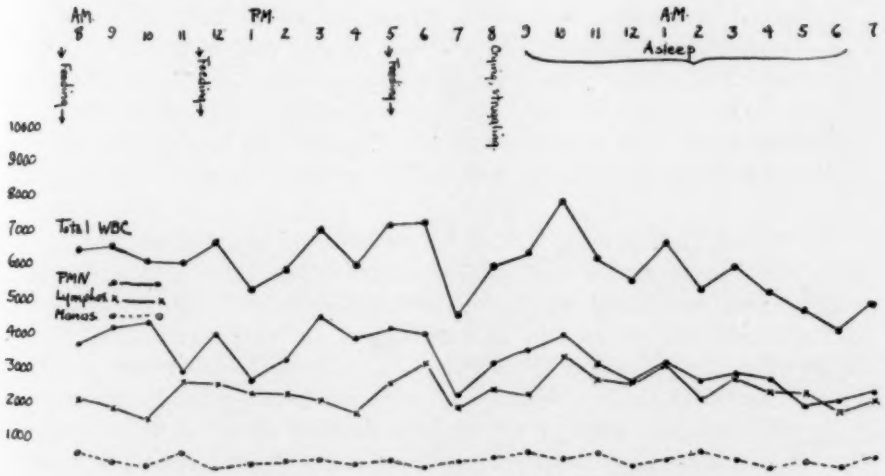

Chart 8.—Variations in leukocyte count in child, aged 13 years.

The eosinophils and basophils were included with the polymorphonuclear neutrophils in our counts.

CONCLUSIONS

1. The times of day and night are factors to be considered in the evaluation of leukocyte counts in infants and in children. Blood counts should be made at the same hours on successive days.

2. Any variation in the leukocyte count which can be interpreted as digestive leukocytosis is inconstant.

3. Whether the facts brought out in our study will be constant in a larger number of cases cannot be stated. (Shaw's study of four adults showed results somewhat similar to ours in children.) The body of the paper contains a summary of detailed observations, which,

briefly stated, were as follows: There was a fluctuation in the total leukocyte count in twenty-four hours, in which the higher counts occurred from about 2 to 4 p. m. and from 12 to 4 a. m., and the lower counts from about 7 to 8 a. m. and from 7 to 10 p. m. In young infants, the curve of lymphocytes followed the total leukocyte count closely; in older children, the number of polymorphonuclear cells more nearly corresponded to the fluctuation in total counts. Both total and differential counts varied greatly in the course of twenty-four hours. In the case of the total leukocyte count, the variation was as much as 175 per cent; the polymorphonuclear cells varied as much as 400 per cent and the lymphocytes, 250 per cent; that is, the highest counts were that much greater than the lowest.

ASTHMA IN CHILDREN

VI. A COMPARATIVE STUDY OF THE SCRATCH AND INTRADERMAL METHODS OF SKIN TESTING *

M. MURRAY PESHKIN, M.D.
AND
A. H. FINEMAN, M.D.
NEW YORK

The existence of human hypersensitiveness to various substances and its detection by means of protein skin tests are now established and generally accepted. The methods largely employed are the scratch and intradermal. The scratch (cutaneous or dermal) method was advocated by Schloss and Walker and the intradermal (intracutaneous) method by Cooke. These methods are so different in regard to technic and interpretation of reactions that the tendency has been to employ one method to the exclusion of the other. It is a moot question as to which method of testing is superior or more reliable, and considerable controversy has resulted.

The proponents of the intradermal method point to the fact that the Mantoux tuberculin test is more delicate than the cutaneous test of Pirquet, and also that the Schick test done by the intradermal method is more reliable and practical than when it is done by the scratch method. Schick, however, found that if a sufficiently concentrated diphtheria toxin was used the scratch test also gave positive reactions. It therefore appears that the whole problem involves the degree of concentration of the test material employed. In these two instances in which only a single substance is used for testing and the toxic material is known, the question of method is readily determined in favor of the intradermal. In the wider field of allergy, however, in which several hundred different substances are used, the active constituents of which are practically unknown and the materials employed empirically standardized, this subject cannot be dismissed so readily. If the protein substances that produce the reactions were known, the intradermal method might prove to be the one of choice. Since they are not known, it is impossible to determine, *a priori,* whether the active constituents are in greater concentration in solution or in powdered extracts. With these thoughts in mind, this study was undertaken to determine not which particular method of testing was easier, quicker, less painful or more practical to perform, but rather which method with the test materials at hand was

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* From the Children's Asthma Clinic, Mount Sinai Hospital.

more reliable and best suited for each protein employed. The comparative incidence of general reactions following the tests was noted; also, the comparative reactions obtained by the scratch method with the dry powders and the fluid extracts; and, so far as possible, the clinical significance of the cutaneous reactions obtained with both methods.

This study is based on 100 patients, 91 of whom had asthma and the remainder, urticaria, angioneurotic edema or eczema. The ages range from 8 months to 14 years. Each child was tested by both the intradermal and the scratch methods in a routine manner with thirty-three corresponding proteins. The dry powdered extracts were employed for the scratch and Coca's fluid extracts for the intradermal tests. The total number of tests performed with each method of testing was 3,265. The Coca solutions were also applied with the scratch method in the majority of instances in which the intradermal test gave a reaction above the normal. All of these children were under observation for at least one year.

PROTEINS USED IN SKIN TESTING

The proteins employed in this series for the scratch test were in powder form and were prepared (with the exception of house dust) under the methods and supervision of R. P. Wodehouse. Before the proteins were used, their activity, so far as possible, was determined by testing subjects known to be definitely sensitive.

Series 1		Series 2	
Timothy	0.01	Wheat	0.28 to 0.49
Ragweed (low)	0.01	Corn	0.23 to 0.49
House dust (stock)	0.20 to 0.40	Rice	0.20 to 0.50
Orris root	0.01 to 0.001	Rye	0.60 to 1.20
Horse epithelium	0.01	Oat	0.16 to 0.30
Horse serum, 1 to 10 dilution.		Buckwheat	0.01
		Milk, 1 to 10 dilution.	
Cat epithelium	0.01	Egg[1]	0.01
Dog epithelium	0.01	Chicken	2.00
Rabbit epithelium	0.01	Beef	2.00
Goat epithelium	0.10	Lamb	2.10
Chicken epithelium	0.10	Pork	2.00
Duck epithelium	0.10	Peanut	0.01
Goose epithelium	0.10	Almond	0.05
Tobacco. Not estimated.		Mustard	0.01
Insecticide. Not estimated.			
Cottonseed	0.005		
Kapok	0.005		
Le Paige's Glue	0.01		

1. This extract contains equal amounts of egg albumin, globulin and ovomucoid.

The corresponding fluid extracts employed for the intradermal tests were kindly furnished by Dr. A. F. Coca of the New York Hospital, who made this work possible. Thirty-three routine extracts arranged in two series were used. The figures following each extract (except horse serum and milk) represent milligrams of nitrogen per cubic centimeter.

The extracts of orris root and the cereal grains were replaced by fresh materials monthly. For children under 3 years of age, extracts ten times weaker were first employed.

TECHNIC OF THE TESTS

The technic of the cutaneous scratch tests and the discussion of skin irritability have been previously described in detail.[2] The immediate reactions were read within thirty minutes from the application of the protein.

After the scratch tests were completed, the corresponding intradermal tests were then performed. With the aid of tuberculin syringes, approximately 0.02 cc. of the fluid extracts were injected intradermally in the forearm, avoiding a site showing any evidence of scarification. The needles employed were ⅜ inch, 27 gage. Three tests were made at one time and placed 1 inch apart. If after five minutes no marked local reaction appeared, three more tests were then made, only six being performed at one sitting. Controls were always made with physiologic sodium chloride solution. The immediate reactions were read within from ten to fifteen minutes from the injection of the extract.

All reactions above the control with both methods of testing were repeated one or more times for confirmation. The average reaction for each protein was the only one recorded.

TYPE OF REACTIONS

The reactions obtained by the two methods are not identical. The readings were made according to the accepted practice for each method.

POSITIVE REACTIONS

The Scratch Reaction:

1. A one plus reaction is a distinct urticarial wheal, 0.05 cm. in diameter, surrounded by a zone of erythema in the presence of a negative control; or a distinct urticarial wheal less than 0.5 cm. in diameter, surrounded by a zone of erythema of 2 or more centimeters; or only a zone of erythema of 2 or more centimeters with little or no elevation around the cut.

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2. Peshkin, M. M., and Rost, W. L.: The Incidence of Protein Sensitization in the Normal Child, Am. J. Dis. Child. **23**:51 (Jan.) 1922.

2. A two plus reaction is an urticarial wheal from 0.6 to 0.7 cm. in diameter, with or without a surrounding zone of erythema.

3. A three plus reaction is an urticarial wheal from 0.8 to 0.9 cm. in diameter, with or without a surrounding zone of erythema.

4. A four plus reaction is an urticarial wheal measuring 1 centimeter or more in diameter with or without a surrounding zone of erythema.

5. All reactions measuring less than the foregoing and more than the control are plus minus and considered positive.

The Intradermal Reaction:

Cooke [3] has divided the skin reaction into three groups: the immediate, delayed and negative reactions. The immediate reactions are classified as marked, moderate or slight and are designated as three, two and one plus respectively. The markedly positive reaction is the only one showing pseudopod projections. This classification no doubt may be satisfactory for practical purposes, but in a study of this nature the size of the various skin reactions must be definitely stated, as follows:

IMMEDIATE REACTIONS

1. A one plus or slightly positive reaction is an urticarial wheal from 0.5 to 1.0 cm. in diameter with a surrounding zone of erythema.

2. A two plus or moderately positive reaction is an urticarial wheal from 1 to 2 cm. in diameter with a surrounding zone of erythema.

3. A three plus or markedly positive reaction is an urticarial wheal more than 1 cm. in diameter with pseudopod projections and a surrounding zone of erythema.

4. A reaction measuring less than the foregoing and more than the control with little or no surrounding zone of erythema is a plus minus reaction.

Delayed reactions were not often observed to occur in this series because the children were not seen twenty-four hours following the tests. These reactions were not included in the statistical report of this study.

A negative reaction with either method of skin testing does not differ in any way from the control.

INTERPRETATION OF THE REACTION

It may be here emphasized that in addition to being trained and experienced with the technic of both methods and the interpretation of their reactions, the workers carrying out this study assumed an impartial attitude toward the controversy.

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3. Cooke, R. A. in Tice's Practice of Medicine, Hagerstown, Md., W. F. Prior Co., 1920.

With reference to the scratch tests, one of us (M. M. P.),[4] in 1923, expressed the opinion that plus minus reactions should not be ignored, thus differing with Rackemann[5] and other early workers in this field. Patients were cited who presented multiple positive and plus minus reactions who got well when one or all of the latter were seriously considered as etiologic factors. The practical importance of not discarding these small reactions was again demonstrated by Peshkin[6] in a recent study in which he stated that "the size of the cutaneous reaction to a substance does not determine its importance in the etiology. The size of the reaction depends on the concentration of the offending substance in the test material used. In the preparation of the test material, the concentration of the etiologic substance may be small and therefore the reaction procured may be comparatively insignificant. Furthermore, the size of the reaction with the same test material on the same person at different times varies greatly . . . Piness and his co-workers[7] published some pertinent facts concerning the varying activity of protein preparations made with various extractives which lend support to these statements."

Definitely positive reactions with the intradermal method, according to the standards employed at the asthma clinic of New York Hospital, include all reactions above one plus. Reactions measuring less than one plus and those not different from the control are regarded as negative. Stronger extracts are employed only in those cases which show indefinite reactions and give a definite history of intolerance to that protein. According to Cooke[8] "where reactions are slight or moderate to the concentrated extracts they are dismissed as of no clinical significance unless they go on to develop delayed reactions . . . Marked reactions are of the greatest importance."

Walker and Adkinson[9] who were among the first, if not the first, to report on the comparative methods of skin testing, concluded that the

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4. Peshkin, M. M.: The Significance of the Protein Skin Reactions in Bronchial Asthma, M. J. & Record **117**:88 (Jan. 17) 1923.

5. Rackemann, F. M.: Skin Tests with Foreign Proteins in Various Conditions, Am. J. M. Sc. **87**:163 (Jan.) 1922.

6. Peshkin, M. M.: Asthma in Children: I. Etiology, Am. J. Dis. Child. **31**:763 (June) 1926.

7. Piness, G.; Miller, H., and Alles, G. A.: Comparative Methods of Protein Extraction with Chemical and Clinical Studies, J. A. M. A. **83**:608 (Aug. 23) 1924.

8. Cooke, R. A.: Cutaneous Reactions in Human Hypersensitiveness, Proc. New York Path. Soc. N. S. **21**:8 (Jan.-May) 1921.

9. Walker, I. C., and Adkinson, J.: Comparison Between Cutaneous and Intradermal Tests in Sensitization of Asthmatic and Hay-Fever Patients, J. M. Research **37**:287 (Nov.) 1917.

intradermal test was much less specific, much too sensitive and therefore erratic. The amount of testing material injected was 0.10 cc.

Larsen et al.[10] compared the intracutaneous test using Coca extracts with corresponding commercial preparations for the scratch method. They reported that in fifteen instances there was no definite reaction with the scratch test, whereas with the intracutaneous method all were positive. These observers, however, considered a scratch reaction less than 1 cm. in diameter as negative.

In a total of 78 comparative tests performed in as many patients of all ages, Brown[11] concluded that the intradermal method was superior to the scratch method because in every patient known to be clinically sensitive to a protein the intradermal test was positive (Coca extracts) and the scratch test (commercial preparations) in only half the number. In a later publication based on this experiment, Brown[12] stated that "there can be no question that the intradermal method used by Cooke and his school is by far the most accurate." The comparative tests were carried out with the following nine substances: horse, dog, cat goose and rabbit epithelium, egg-white, wheat, milk and casein. Brown, however, interpreted the scratch reactions by the intradermal standards.

Comparative studies were also made by Schloss,[13] Strickler[14] and others. These reports dealt mainly with a single group of proteins, such as food or pollen, and the materials employed for testing were not similar to those used in this study.

The comparative tests recorded in this series were begun in January, 1924, and completed in June, 1925. The asthma group and the dermatoses group will be considered separately. The asthma group will be further considered under two subgroups: sensitization to the (1) inhalant and (2) food proteins.

(A) ASTHMA GROUP

Sensitization to the Inhalant Proteins.—Table 1 shows the comparative results of the scratch and intradermal tests with the common inhalant proteins. Every reaction above the control with both methods is recorded.

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10. Larsen, N. P.; Paddock, R., and Alexander, H. L.: Bronchial Asthma and Allied Conditions. Clinical and Immunological Observation, J. Immunol. **7**:81 (March) 1922.

11. Brown, A.: Studies in Specific Hypersensitiveness: I. The Diagnostic Cutaneous Reaction in Allergy. Comparison of the Intradermal Method (Cooke) and the Scratch Method (Schloss), J. Immunol. **7**:97 (March) 1922.

12. Brown, A.: Present Day Treatment of Asthma, M. J. & Record **118**:333 (Sept. 19) 1923.

13. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433 (June) 1920.

14. Strickler, A.: The Results in Food Anaphylaxis Obtained by Cutaneous and Intracutaneous Methods, J. A. M. A. **79**:808 (Sept. 2) 1922.

Sensitization to House Dust.—The house dust used for the scratch test in the early part of this series consisted of three powdered extracts prepared from the dusts from three separate homes. The patients were tested with all three extracts. The dust giving the maximum skin reaction was the only one recorded.[15] Later, an active polyvalent stock house dust was employed. This preparation proved to be more satisfactory than the three single dusts used. The stock dust (Coca) used for the intradermal test was of the highest available concentration.

TABLE 1.—*Corresponding Reactions with the Scratch and Intradermal Methods to House Dust, Rabbit Hair, Horse Dander, Ragweed and Timothy*

Scratch Method		Intradermal Method					
Skin Reactions	Number of Reactions		Negative			Positive	
			—	±	+	++	+++
House Dust							
±	16		0	4	10	2	0
+	17		0	0	8	6	3
++	3		0	0	3	0	0
+++	1		0	0	1	0	0
++++	2		0	0	1	1	0
Positive	39		0	4	23	9	3
Negative	52		17	14	19	2	0
Total	91		17	18	42	11	3
Rabbit Hair							
±	7		5	1	1	0	0
+	7		5	0	0	2	0
++	5		0	1	2	2	0
++++	13		0	0	5	5	3
Positive	32		10	2	8	9	3
Negative	59		58	1	0	0	0
Total	91		68	3	8	9	3
Horse Dander							
±	15		7	4	4	0	0
+	3		1	0	2	0	0
++	4		1	0	2	0	1
++++	2		0	0	0	2	0
Positive	24		9	4	8	2	1
Negative	67		64	3	0	0	0
Total	91		73	7	8	2	1
Ragweed							
±	5		1	1	2	1	0
+	5		1	2	1	1	0
++	2		1	0	1	0	0
Positive	12		3	3	4	2	0
Negative	79		73	5	1	0	0
Total	91		76	8	5	2	0
Timothy							
±	1		0	1	0	0	0
Positive	1		0	1	0	0	0
Negative	90		88	2	0	0	0
Total	91		88	3	0	0	0

Thirty-nine patients gave positive skin reactions to house dust with the scratch method; four of these reactions were negative by intradermal test. With the intradermal method, two patients gave definitely positive reactions, and nineteen gave one plus reactions; in all of these patients, the scratch test was negative.

House dust played a definite etiologic rôle in asthma in only five children. All of these children gave a one plus intradermal reaction to dust, and the corresponding scratch reactions with the dry powder were

15. Dry powdered house dust extract is not commercially obtainable.

negative in two, plus minus in one, one plus in another and four plus in the remaining case.

Thus, from the clinical standpoint, the one plus intradermal reaction with house dust must be considered as a definitely positive reaction in spite of the fact that this reaction is not infrequently found in normal subjects. The intradermal method of testing for house dust appears to be superior to the scratch test.

Sensitization to Rabbit Hair.—Every patient with definitely positive reactions to rabbit hair by the intradermal method also gave a positive reaction with the dry powder. However, of the thirty-two children who gave positive reactions with the scratch method, twelve of these, or 37 per cent, gave negative reactions by the intradermal test, eight gave a one plus and the remainder gave definitely positive reactions.

Rabbit hair played an existing rôle in the causation of asthma in twenty-one patients. The removal of the hair from their homes was followed by complete or marked relief from asthma in all. Three patients gave plus minus and three one plus scratch reactions. In five of these six patients, the corresponding intradermal reactions were negative. Fourteen patients gave from two to four plus scratch reactions; of these, the corresponding intradermal reactions were plus minus in 1, one plus in 5, two plus in 5 and three plus in 3.

It is therefore evident that with the materials employed, the determination of sensitiveness to rabbit hair is most dependable and reliable with the scratch method.

Sensitization to Horse Dander.—Every patient reacting positively to horse dander with the intradermal method also reacted positively with the scratch test. Twenty-four patients gave positive reactions with the scratch method. Thirteen of these, or 54 per cent, gave negative reactions to the intradermal test, eight gave one plus and only three gave definitely positive reactions.

Horse dander played a contributory rôle in one case and was a sole factor in the causation of asthma in another. One showed a plus minus reaction with the scratch test and a negative reaction with the intradermal test. The other gave a four plus reaction to the scratch and a two plus to the intradermal method.

Thus, with the material at hand the scratch method of determining sensitivity to horse dander is by far more dependable and reliable than the intradermal.

Sensitization to Pollen.—Ragweed played an etiologic rôle in the causation of symptoms in eight patients. Three patients gave a plus minus scratch reaction; the corresponding intradermal reactions were plus minus in one and two plus in two. Four patients gave one plus scratch reactions; the corresponding intradermal reactions were negative,

plus minus, one plus and two plus, respectively. One patient gave a two plus with the scratch and a negative reaction with the intradermal method. The conjunctival test with powdered ragweed in all of these patients was strongly positive.

In four patients, there was a history of negative pollen reactions. The scratch reactions in two were plus minus, and the corresponding intradermal reactions were negative and one plus, respectively. In another case, the scratch reaction was one plus and the intradermal plus minus. In the fourth case, the scratch reaction was two plus and the intradermal one plus. In the latter case, the conjunctival test was also positive.

Six children with histories of negative pollen reactions also reacted negatively to short ragweed with the scratch method (table 1). Five of these gave a plus minus and the remaining one a one plus reaction with the intradermal method. The conjunctival test with powdered ragweed on three of these patients was performed with negative results.

Three patients showed a plus minus intradermal reaction to timothy, and the corresponding scratch test with the dry powder was positive in only one case. All of these children gave histories of a negative pollen reaction.

It is of interest to note that in this series, there were four children who exhibited negative reactions by the scratch and intradermal tests but showed definitely positive reactions by the conjunctival method to the powdered ragweed pollen. One of these children reacted similarly to timothy. All of these patients gave histories of positive pollen reactions and subsequently were found to be negative also by the intradermal test to a 1 : 50 solution of pollen (0.25 mg. of nitrogen per cubic centimeter).

Conjunctival tests with dry pollen should be performed only when the scratch test is negative in patients with histories of positive or suspicious pollen reactions. In this series, such a rule was not followed for obvious reasons.

The scratch method for determining pollen sensitivity as shown from the foregoing is more reliable than the intradermal. There exists a small group of subjects sensitive to pollens who are refractory to both methods of skin testing and in whom a positive diagnosis can be easily made with the dry powder by the conjunctival method.

Sensitization to Cat and Dog Dander.—The corresponding scratch and intradermal reactions to cat and dog dander are shown in table 2.

The children reacting to cat and dog dander subjected themselves to casual exposure to the animal without manifesting any symptoms.

From the standpoint of testing alone, the scratch method with cat and dog dander is superior to the intradermal.

Sensitization to Feathers.—The corresponding scratch and intradermal reactions to chicken, duck and goose feathers are shown in table 3.

In none of these patients (table 3) with positive reactions to chicken feathers was the sensitization etiologic. It has been previously shown [16]

TABLE 2.—*Corresponding Reactions with the Scratch and Intradermal Methods to Cat and Dog Dander*

Scratch Method		Cat Dander				
		Intradermal Method				
		Negative			Positive	
Skin Reactions	Number of Reactions	—	±	+	++	+++
±	9	5	2	1	1	0
+	2	1	1	0	0	0
Positive	11	6	3	1	1	0
Negative	80	76	4	0	0	0
Total	91	82	7	1	1	0
		Dog Dander				
±	4	3	0	1	0	0
+	1	1	0	0	0	0
Positive	5	4	0	1	0	0
Negative	86	72	10	4	0	0
Total	91	76	10	5	0	0

TABLE 3.—*Corresponding Reactions with the Scratch and Intradermal Methods to Chicken, Duck and Goose Feathers*

		Chicken Feathers				
		Intradermal Method				
		Negative			Positive	
Skin Reactions	Number of Reactions	—	±	+	++	+++
±	10	3	2	4	1	0
+	2	1	1	0	0	0
Positive	12	4	3	4	1	0
Negative	79	50	16	9	3	1
Total	91	54	19	13	4	1
		Duck Feathers				
±	14	10	2	2	0	0
+	2	0	2	0	0	0
Positive	16	10	4	2	0	0
Negative	75	66	6	3	0	0
Total	91	76	10	5	0	0
		Goose Feathers				
±	14	4	9	1	0	0
+	1	0	0	1	0	0
Positive	15	4	9	2	0	0
Negative	76	65	9	2	0	0
Total	91	69	18	4	0	0

that this class of children does not come in contact with chicken feathers except for casual exposure. It will be seen from table 3 that chicken feather protein gives from two to three times more intradermal slightly positive (one plus) reactions than duck or goose feathers. Since this reaction played no part in the causation, it is reasonable to suspect that in the fluid extract of chicken feathers there exists some irritating nonspecific substance responsible for these reactions. From a com-

16. Peshkin (footnotes 4 and 6).

parative testing standpoint, however, the intradermal method for determining sensitiveness to chicken feathers must be recorded as being the superior method.

In all of the patients giving positive reactions to duck or goose feathers, a history of intolerance to these substances was lacking.

TABLE 4.—*Corresponding Reactions with the Scratch and Intradermal Methods to Goat Hair, Orris Root, Tobacco, Pyrethrum (Insecticide), Cottonseed, Kapok and Horse Serum*

Scratch Method		Intradermal Method				
Skin Reactions	Number of Reactions	Negative			Positive	
		—	±	+	++	+++
Goat Hair						
±	6	4	2	0	0	0
+	3	2	1	0	0	0
++	1	1	0	0	0	0
++++	1	0	0	0	1	0
Positive	11	7	3	0	1	0
Negative	80	57	13	7	3	0
Total	91	64	16	7	4	0
Orris Root						
±	2	0	2	0	0	0
+	1	1	0	0	0	0
Positive	3	1	2	0	0	0
Negative	88	84	4	0	0	0
Total	91	85	6	0	0	0
Tobacco						
Positive	0	0	0	0	0	0
Negative	60	40	8	11	1	0
Total	60	40	8	11	1	0
Pyrethrum (Insecticide)						
±	2	0	1	1	0	0
+	1	1	0	0	0	0
Positive	3	1	1	1	0	0
Negative	88	65	19	4	0	0
Total	91	66	20	5	0	0
Cottonseed						
±	1	1	0	0	0	0
+++	1	0	0	1	0	0
Positive	2	1	0	1	0	0
Negative	89	85	3	1	0	0
Total	91	86	3	2	0	0
Kapok						
±	4	3	1	0	0	0
+	1	0	0	1	0	0
Positive	5	3	1	1	0	0
Negative	85	85	0	0	0	0
Total	90	88	1	1	0	0
Horse Serum *						
±	1	0	1	0	0	0
+	1	0	0	0	0	1
Positive	2	0	1	0	0	1
Negative	89	73	8	7	1	0
Total	91	73	9	7	1	1

* Included here for convenience.

However, from a standpoint of testing, the scratch method for determining sensitiveness to these feathers is more reliable than the corresponding intradermal method.

Sensitization to Other Inhalants.—The reaction to Le Paige's glue was negative in all cases with either method of skin testing.

The corresponding scratch and intradermal reactions to goat hair, orris root, tobacco, pyrethrum (insecticide), cottonseed, kapok and horse serum are shown in table 4.

Neither horse serum nor the inhalants listed in table 4 was an etiologic factor of asthma in a single case.

From a testing standpoint, the method of choice for demonstrating sensitization to goat hair is the scratch. In the presence of a negative scratch reaction the intradermal test will give a definitely positive reaction in a small percentage of the cases. This applies also to horse serum.

Cottonseed is best demonstrated by the scratch method, which was borne out by subsequent comparative tests.

The suspicion that tobacco and pyrethrum were responsible for many pseudoreactions with the intradermal tests has been confirmed in this series. However, tobacco gave one definitely positive reaction with the

TABLE 5.—*Summary of the Corresponding Reactions to the Inhalant Substances with the Scratch and Intradermal Tests*

Scratch Method		Intradermal Method				
Skin Reactions	Number of Reactions	Negative			Positive	
		—	±	+	++	+++
+	45	13	6	13	9	4
++	15	3	1	8	2	1
+++	2	0	0	1	1	0
++++	18	0	0	6	9	3
Plus Reactions	80	16	7	28	21	8
Plus Minus Reactions	113	47	34	27	5	0
Positive	193	63	41	55	26	8
Negative	1413	1209	125	68	10	1
Total	1606	1272	166	123	36	9

intradermal and none with the scratch test, while with pyrethrum, the scratch test is the method of choice.

Table 5 is a summary of the corresponding reactions to the inhalant substances with both methods of skin testing.

From table 5, it can be observed that of 1,413 negative scratch inhalant reactions, the corresponding intradermal reactions were definitely positive (++ and +++) in 0.78 per cent, one plus in 4.8 per cent and negative (— and ±) in 94.41 per cent. Of the total positive scratch reactions (± to ++++), the corresponding intradermal reactions were definitely positive in 17.6 per cent, one plus in 28.5 per cent and negative in 53.9 per cent.

FOOD PROTEINS

Table 6 shows the comparative results of the cereal grains with the scratch and intradermal tests.

The positive reactions to the cereal grains recorded in table 6 did not enter into the causation of asthma in a single case.

Table 7 shows the comparative results to milk and egg with the scratch and intradermal tests.

None of the children reacting to milk (table 7) gave a history of intolerance.

TABLE 6.—*Corresponding Reactions with the Scratch and Intradermal Methods to Cereal Grains*

Scratch Method		Wheat	Intradermal Method				
Skin Reactions	Number of Reactions		Negative			Positive	
			—	±	+	++	+++
±	8		2	0	5	1	0
+	2		1	0	1	0	0
Positive	10		3	0	6	1	0
Negative	81		53	20	6	2	0
Total	91		56	20	12	3	0
		Corn					
±	1		0	0	1	0	0
+	1		0	0	0	1	0
Positive	2		0	0	1	1	0
Negative	89		60	20	8	1	0
Total	91		60	20	9	2	0
		Rice					
±	1		0	1	0	0	0
+	1		0	0	1	0	0
Positive	2		0	1	1	0	0
Negative	89		56	20	13	0	0
Total	91		56	21	14	0	0
		Rye					
Positive	0		0	0	0	0	0
Negative	91		82	5	4	0	0
Total	91		82	5	4	0	0
		Oat					
±	3		3	0	0	0	0
Positive	3		3	0	0	0	0
Negative	88		76	7	5	0	0
Total	91		79	7	5	0	0
		Buckwheat					
Positive	0		0	0	0	0	0
Negative	91		88	2	1	0	0
Total	91		88	2	1	0	0

TABLE 7.—*Corresponding Reactions with the Scratch and Intradermal Methods to Milk and Egg*

Scratch Method		Milk	Intradermal Method				
Skin Reaction	Number of Reactions		Negative			Positive	
			—	±	+	++	++++
±	1		0	1	0	0	0
Positive	1		0	1	0	0	0
Negative	90		78	9	3	0	0
Total	91		78	10	3	0	0
		Egg					
±	4		3	0	0	1	0
+	1		0	1	0	0	0
++	1		0	0	0	1	0
++++	2		0	0	0	2	0
Positive	8		3	1	0	4	0
Negative	83		76	6	1	0	0
Total	91		79	7	1	4	0

A history of intolerance to egg was obtained in three cases. One child gave a plus minus scratch and a two plus intradermal reaction. The other two gave four plus scratch reactions and two plus intradermal.

Table 8 shows the comparative results to chicken, beef, lamb and pork with both methods of skin testing.

Only one child gave a history of intolerance to the meats and gave positive reactions to the whole biologic group. The scratch reactions varied from one to two plus; the intradermal reactions were all three plus. In this case, the intradermal tests were followed within five minutes by a violent general reaction.

TABLE 8.—*Corresponding Reactions with the Scratch and Intradermal Methods to Chicken, Beef, Lamb and Pork*

Scratch Method		Chicken	Intradermal Method				
			Negative			Positive	
Skin Reaction	Number of Reactions		—	±	+	++	+++
+	1		0	0	0	1	0
++	1		0	0	0	0	1
Positive	2		0	0	0	1	1
Negative	89		49	33	5	2	0
Total	91		49	33	5	3	1
		Beef					
+	1		0	0	0	0	1
Positive	1		0	0	0	0	1
Negative	90		75	11	4	0	0
Total	91		75	11	4	0	1
		Lamb					
±	1		1	0	0	0	0
+	1		0	0	0	0	1
Positive	2		1	0	0	0	1
Negative	89		69	17	3	0	0
Total	91		70	17	3	0	1
		Pork					
±	1		0	1	0	0	0
Positive	1		0	1	0	0	0
Negative	90		81	9	0	0	0
Total	91		81	10	0	0	0

TABLE 9.—*Corresponding Reactions with the Scratch and Intradermal Methods to Peanut, Almond and Mustard*

Scratch Method		Peanut	Intradermal Method				
			Negative			Positive	
Skin Reaction	Number of Reactions		—	±	+	++	+++
Positive	0		0	0	0	0	0
Negative	90		80	1	0	0	0
Total	90		80	1	0	0	0
		Almond					
±	1		0	1	0	0	0
++++	1		0	0	0	1	0
Positive	2		0	1	0	1	0
Negative	89		86	2	1	0	0
Total	91		86	3	1	1	0
		Mustard					
±	3		3	0	0	0	0
++	2		0	1	1	0	0
+++	1		1	0	0	0	0
Positive	6		4	1	1	0	0
Negative	83		80	2	1	0	0
Total	29		84	3	2	0	0

Table 9 shows the comparative results to tests with peanut, almond and mustard.

None of the cases reacting to nut with either method (table 9) gave a history of intolerance.

Mustard acts almost entirely as an inhalant. One of the patients who gave a two plus scratch and a corresponding one plus intradermal reaction gave a definite history of intolerance when exposed to mustard.

Table 10 is a summary of the corresponding reactions to the various food substances with both methods of skin testing.

From table 10, it can be observed that of 1,322 negative scratch food tests, the corresponding intradermal reactions were definitely positive (++ and +++) in 0.38 per cent, one plus in 4.16 per cent and negative (— and ±) in 95.46 per cent. Of the total positive scratch tests, the corresponding intradermal tests were definitely positive in 27.5 per cent, one plus in 22.5 per cent and negative in 50 per cent.

The scratch method of skin testing is more sensitive to egg and mustard and less sensitive to chicken than the intradermal tests. With the remaining foods, the intradermal tests do not appear to have any special advantage over the scratch method, with the possible exception of wheat and corn.

TABLE 10.—*Summary of the Corresponding Reactions to the Food Substances with the Scratch and Intradermal Tests*

Scratch Method		Intradermal Method				
Skin Reactions	Number of Reactions	Negative			Positive	
		—	±	+	++	+++
+	8	1	1	2	2	2
++	4	0	1	1	1	1
+++	1	1	0	0	0	0
++++	3	0	0	0	3	0
Plus Reactions	16	2	2	3	6	3
Plus Minus Reactions	24	12	4	6	2	0
Positive	40	14	6	9	8	3
Negative	1322	1098	164	55	5	0
Total	1362	1112	170	64	13	3

(B) DERMATOSES GROUP

The dermatoses group was composed of nine children ranging in age from 1½ to 9 years. One of these children had eczema and the remainder, recurrent urticaria. Three of the children with urticaria also had angioneurotic edema. All the children of the group, except one, first developed the rash after the age of 1½ years.

All of these children reacted negatively to the scratch tests. With the intradermal method, four reacted negatively. The remaining five reacted to the intradermal tests as follows: dust plus minus reactions in three and one plus in two children. One of these children also gave plus minus reactions to wheat, tobacco, pyrethrum and goose epithelium and another plus minus reactions to horse serum and one plus to pork. None of these reactions were responsible for any manifestations of allergy. Incidentally, it is of interest to note that the intradermal plus minus and one plus dust reactions were obtained in more than one half of these cases.

GENERAL REACTIONS FOLLOWING SKIN TESTS

Cooke,[17] employing the intradermal test exclusively in a large series of patients of all ages, reported that the incidence of general (constitutional) reactions following test injections was 2 per cent. Two per cent of the cases in our series also exhibited general reactions following intradermal injections. One occurred in a boy, aged 9, who showed many positive reactions including chicken, beef and lamb with the scratch method. The intradermal tests performed with these meat extracts caused a violent attack of asthma with generalized urticaria within five minutes. Repeated injections of epinephrine hydrochloride were necessary to control these acute symptoms. The scratch tests performed at one sitting resulting in ten positive reactions including the meats did not produce the slightest evidence of an immediate or delayed general reaction in the same case. It may be mentioned here that about 400 children have been tested in our clinic with the dry powders without the occurrence of a single general reaction.

Delayed general reactions resulting in asthma following the intradermal tests could not be satisfactorily determined. In a small group of children, the asthma was observed to become definitely aggravated during the course of the intradermal tests. On the other hand in some cases, especially in those of the nonsensitive group, the asthma was temporarily lessened or had cleared, probably as a result of the substances injected. Such effects were not noted with the scratch tests.

Cooke [17] stated that "the general reactions following intradermal tests are due to a more potent extract than is generally used in the scratch test" and bases this contention on the reports of Brown [11] and Larsen et al.[10] Peshkin [6] attributes the rarity of occurrence of a general reaction following a scratch test, properly performed, to the edema accompanying a positive reaction which seals the cut and prevents further absorption of the protein. By virtue of its being a scratch test, there is the slowest possible absorption of protein, and the reaction thereby becomes purely local in its effect. It has been previously stated that when a series of skin tests was completed, all the positive reactions were repeated for confirmation. As a result of this procedure, as many as ten or more positive reactions have been elicited at one sitting without the slightest evidence of an immediate or delayed general reaction. It therefore appears that the main reason for the occurrence of general reactions after intradermal tests is not the greater potency of the fluid extracts but because it is an injection test and as such the absorption of the protein is beyond control.

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17. Cooke, R. A.: Studies in Specific Hypersensitiveness: III. On Constitutional Reactions; The Dangers of the Diagnostic Cutaneous Test and Therapeutic Injection of Allergens, J. Immunol. **7**:119 (March) 1922.

THE SCRATCH TESTS WITH THE DRY POWDERS AND FLUID EXTRACTS

Table 11 shows a summary of the comparative reactions obtained with corresponding dry powders and routine fluid extracts by the scratch method in 371 instances. All these gave reactions ranging from plus minus to three plus with the intradermal method.

Of 117 positive reactions with the dry powder, the corresponding scratch reactions with the routine fluid extracts were negative in 79.5 per cent and positive in 20.5 per cent.

Of 254 negative reactions with the dry powder, the corresponding scratch reactions with the fluid extracts were negative in 97 per cent and positive in only 3 per cent.

TABLE 11.—*Comparative Reactions by the Scratch Method with Dry Powders (Wodehouse) and Routine Fluid Extracts (Coca)*

Dry Powder		Fluid Extract Corresponding Reactions					
Size of Reaction	Number of Reactions	—	±	+	++	+++	++++
±	52	45	4	3	0	0	0
+	21	16	4	0	1	0	0
++	13	8	2	1	1	1	0
+++	6	6	0	0	0	0	0
++++	25	18	3	3	0	0	1
Positive	117	98	13	7	2	1	1
Negative	254	246	7	1	0	0	0
Total	371	339	20	8	2	1	1

It is of interest to note here that the dry powdered house dust extract gave thirty-nine positive reactions ranging from plus minus to four plus, while the concentrated fluid extract gave only ten positive scratch reactions ranging from plus minus to one plus.

SUMMARY

Table 12 shows a summary of the corresponding reactions to the various inhalant and food substances with the scratch and intradermal methods in children with asthma and the dermatoses.

From table 12, it is evident that those workers who use only patients showing definitely positive skin reactions with the intradermal method as subjects for comparison with extracts of any character by the scratch method have failed to make a true comparison between the two methods and have also missed inherent values in the scratch test.

It is of interest to note that as the positive skin reactions with the scratch method become stronger the incidence of the corresponding negative and plus-minus intradermal reactions decreases and also that the one plus reactions are not materially changed. When the scratch

reactions are strongly positive (+++ and ++++), the corresponding intradermal negative and plus minus reactions disappear except in one instance.

Thirty-eight patients in the entire series reacted negatively with the scratch method. Fifteen of these also gave negative reactions with the intradermal method and in twenty-three, only plus minus or one plus reactions were obtained. The substances producing these reactions did not play a contributory or etiologic factor in the causation of symptoms in a single case. No patients were encountered who gave negative reactions with the scratch method and definitely positive reactions with the intradermal method.

TABLE 12.—*Summary of the Corresponding Reactions to Thirty-Three Inhalant and Food Proteins with the Scratch and Intradermal Tests in Ninety-One Children with Asthma and Nine with Eczema, Urticaria Angioneurotic Edema*

Scratch Method		Intradermal Method									
		Number of Reactions					Percentage of Reactions				
		Negative		Positive			Negative		Positive		
Skin Reactions	Number of Reactions	—	±	+	++	+++	—	±	+	++	+++
+	53	14	7	15	11	6	27	13	28	21	11
++	19	3	2	9	3	2	16	10	48	16	10
+++ and ++++	24	1	0	7	13	3	4	0	29	54	13
One to four plus	96	18	9	31	27	11	18.75	9.38	32.29	28.12	11.46
Plus minus	137	59	38	33	7	0	43.06	27.74	24.09	5.11	0.00
Total Positive	233	77	47	64	34	11	33.05	20.17	27.47	14.59	4.72
Negative	3032	2593	297	126	15	1	85.52	9.80	4.15	0.50	0.03
Total tests	3265	2670	344	190	49	12	81.77	10.55	5.81	1.50	0.37

Sixty-two cases showed positive reactions to one or more proteins with the scratch method and of these, thirteen were plus minus. With the intradermal method, twenty-six of these cases gave reactions no greater than one plus and thirty-six, two and three plus.

The treatment in all the cases was first based on the skin reactions elicited by the scratch method. When no relief from symptoms was obtained, any further information elicited by the intradermal test (reactions from plus minus up) was taken into consideration. In not a single case was treatment based on this additional information of any value.

COMMENT

The results of this investigation are in striking contrast to the reports on this subject in the literature. This may be due to the fact that the dry powders used in this series were more concentrated and potent than the extracts used in former years; that the skin tests with both methods were properly performed and rationally interpreted, and that the subjects tested comprised an unselected group of children.

When the results of this study and the classification and interpretation given by Cooke and his co-workers to the intradermal reactions are considered, credit must be given to Walker for his early observation that the intradermal method gave many pseudoreactions or nonspecific reactions and for his persistence in maintaining this point throughout the controversy.

CONCLUSIONS

1. Ninety-one children with asthma and nine with eczema, urticaria or angioneurotic edema, ranging in age from 8 months to 14 years, were tested by the scratch and intradermal methods with thirty-three corresponding proteins. Dry powdered extracts (Wodehouse) were employed for the scratch and routine fluid extracts (Coca) for the intradermal tests. The fluid extracts were also applied with the scratch method when the intradermal test gave a reaction above the control. All of these children were under observation for at least one year.

2. In interpreting the reactions obtained with the scratch method, all reactions above the control were considered positive. With the intradermal method, although all reactions above the control were recorded, only reactions of two plus or more were considered definitely positive. This interpretation is in accordance with accepted standards for this method (Cooke et al.). However, it appears that one plus reactions should not be entirely ignored in spite of the fact that they are most frequently nonspecific.

3. Thirty-eight children of the entire series reacted negatively with the scratch method. With the intradermal method, fifteen children gave negative reactions, and in twenty-three the reactions obtained were plus minus and one plus only.

Sixty-two children reacted positively to the scratch method. With the intradermal method, twenty-six patients gave reactions not larger than one plus and in thirty-six two and three plus.

No patients were encountered who gave definitely positive reactions with the intradermal method and negative reactions with the scratch method.

4. The total number of negative reactions obtained with the scratch method were 3,032. The corresponding reactions with the intradermal method were definitely positive (++ and +++), in 0.53 per cent; one plus, in 4.15 per cent, and negative (— and ±), in 95.32 per cent.

The total number of positive reactions (± to ++++) obtained with the scratch method were 233. The corresponding reactions with the intradermal method were definitely positive in 19.31 per cent; one plus in 27.47 per cent and negative in 53.22 per cent.

5. Pseudoreactions or nonspecific reactions were common with the intradermal method. Practically all the plus minus and a majority of

the one plus reactions were of this character. The nonspecific reactions occurred most commonly with the following substances in their order of frequency; house dust, chicken meat, rice, wheat, chicken epithelium, tobacco, corn, pyrethrum (insecticide), goose and goat epithelium and lamb. Pseudoreactions with the scratch method were relatively infrequent.

6. Four children gave a history of positive pollen reactions and negative ragweed reactions with both methods of testing (the fluid extract for the intradermal test was employed up to a concentration of 0.25 mg. of nitrogen per cubic centimeter); they gave positive reactions by the conjunctival test to the dry powder. The latter method of testing has been shown by Peshkin [6] to be a rapid, safe and reliable method of demonstrating sensitiveness to pollen in patients refractory to skin tests.

7. General reactions occurred in 2 per cent of the patients tested with the intradermal method and none with the scratch method.

8. The scratch test is superior to the intradermal test for the following substances: rabbit hair, horse dander, ragweed, cottonseed, duck and goose feathers, cat and dog hair, mustard and egg-white.

The intradermal test is superior to the scratch test for the following substances: house dust, chicken epithelium, chicken meat, wheat and corn. In the presence of negative scratch reactions to horse serum and goat hair, the intradermal method, in a small percentage of the cases, will reveal definitely positive reactions.

9. From the standpoint of safety and the determination of etiologic sensitizations, the scratch method would appear to be superior as a routine procedure for testing. The value of the intradermal method cannot be ignored. One method should not be employed to the exclusion of the other.

562 West End Avenue.
645 West End Avenue.

PARATHYROID THERAPY IN INFANTILE TETANY

REPORT OF FOUR CASES*

A. H. GIBSON, M.D.
ELKHART, IND.

Since the isolation and description of the physiologic action of the active principle of the parathyroid glands by Collip and his associates,[1] only seven cases have been reported in which the active parathyroid extract has been used in the treatment of infantile tetany. In a recent summary of parathyroid therapy by McCann,[2] references to the reports of five cases of infantile tetany are included. Since that time, reports of two cases have been published. The first case was reported in the literature by Collip and Leitch,[3] prior to the publication of Collip's article [1] on the method of extracting the parathyroids. The remaining six cases were reported by Hoag, Rivkin et al.[4] All the patients reported are thought to have been successfully treated with parathyroid extract, but the relation of the rise in serum calcium to the temperature is not stressed in any case.

In the four cases reported here, it is apparent from the charts that there is a definite relation between the rise in serum calcium and the drop in temperature. Whether or not the drop in temperature coincident with the recovery from infection is intimately related to the administration of parathyroid extract, brings up the entire question of the mechanism operating in the reduction of serum calcium in infantile tetany. The cases are too few for generalization. Suffice it to state

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* From the Department of Pediatrics of the Rush Medical College of the University of Chicago.

* Cases 1 and 2 are from the clinical services, respectively, of Drs. A. L. Kastner and Lorenzo Boorse at the Milwaukee Children's Hospital. Cases 3 and 4 are from the clinical service of Dr. Clifford G. Grulee at the Presbyterian Hospital of the City of Chicago.

1. Collip, J. B.: The Extraction of a Parathyroid Hormone which will Prevent or Control Parathyroid Tetany, and Which Regulates the Level of Blood Calcium, J. Biol. Chem. **63**:395 (March) 1925; The Parathyroid Glands, Medicine **5**:1 (Feb.) 1926.

2. McCann, W. S.: Parathyroid Therapy, J. A. M. A. **88**:566 (Feb. 19) 1927.

3. Collip, J. B., and Leitch, D. B.: A Case of Tetany Treated with Parathyrin, Canad. M. A. J. **15**:59 (Jan.) 1925.

4. Hoag, L. A., and Rivkin, Helen: Treatment of Infantile Tetany with Parathyroid Extract, J. A. M. A. **86**:1343 (May 1) 1926. Hoag, L. A.; Rivkin, Helen, et al: Effect of Potent Parathyroid Extract on Calcium Balance in Infants, Am. J. Dis. Child. **33**:910 (June) 1927.

here that this mechanism is probably a more complicated problem than a simple hypofunction of the parathyroid glands. My object in this paper is not to discuss the etiology of infantile tetany, but only to call attention to a few simple facts observed in the treatment of these four patients with parthyroid extract.

Hoag and Rivkin [4] recommend a dosage of five units [5] per kilogram of body weight for each milligram of rise in serum calcium desired. The total dose is administered in equal fractions hypodermically, at four to six hour intervals, over a period of twenty-four to thirty-six hours. The patients described in this paper were treated on this basis. The determinations of serum calcium were made with Clark and Collip's modification of the Tisdall method,[6] and those of serum phosphorus with Benedict and Theis's modification of the molybdic method.[7] Parathyroid extract-Collip was used in all cases.

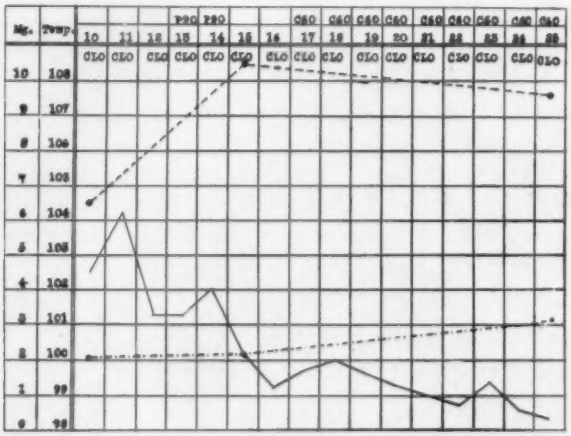

Chart 1 (case 1).—Data of administration of parathyroid extract. In this chart and in charts 2, 3 and 4, the solid line indicates the rectal temperature (Fahrenheit); the dotted line, milligrams of calcium per hundred cubic centimeters of blood serum, and the dot and dash line, milligrams of phosphorus per hundred cubic centimeters of blood serum. In this chart, P 90 indicates parathyroid extract-Collip, 90 units; C 60, calcium chloride, 60 grains; CLO, cod liver oil, 3 drams.

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5. A unit is equivalent to "one hundredth of the amount of extract which will produce an average increase of 5 mg. in the blood serum calcium of normal dogs of approximately 20 Kg. weight, over a period of fifteen hours" (Collip).

6. Clark, E. P., and Collip, J. B.: A Study of Tisdall Method for the Determination of Blood Serum Calcium with a Suggested Modification, J. Biol. Chem. **63**:461 (March) 1925.

7. Benedict, S. R., and Theis, R. C.: A Modification of the Molybdic Method for the Determination of Inorganic Phosphorus in Serum, J. Biol. Chem. **61**:63 (Aug.) 1924.

REPORT OF CASES

CASE 1.—F. M., a boy, aged 13 months, weighing 9 Kg., was admitted to the Milwaukee Children's Hospital on May 10, 1926, with clinical evidence of bronchopneumonia, rickets and infantile tetany, including carpopedal spasm, inspiratory crow, positive Chvostek's sign, a temperature of 102.6 F. and a blood serum calcium of 6.6 mg. per hundred cubic centimeters. The following day the temperature rose to 104.2 F., and on May 13 and May 14, ninety units of parathyroid extract, in three doses of thirty units, was given subcutaneously at six hour intervals. On May 15, the temperature had dropped to 100.2 F., and the serum calcium had risen to 10.69 mg. per hundred cubic centimeters. The clinical evidence of tetany had disappeared. The temperature continued to drop and was normal by May 25, at which time the serum calcium was 9.66 mg. per hundred cubic centimeters. Cod liver oil, one teaspoonful three times daily, was given throughout the hospital stay, and may have had some influence on the calcium metabolism through its action in increasing intestinal absorption of calcium. From May 17 to May 25, 30 grains (1.95 Gm.) of calcium chloride was given orally three times daily.

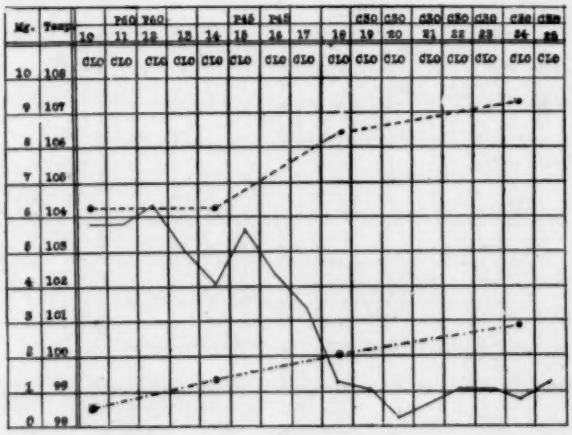

Chart 2 (case 2).—Data of administration of parathyroid extract. P 60 indicates parathyroid extract-Collip, 60 units; P 45, parathyroid extract-Collip, 45 units; C 30, calcium chloride, 30 grains; CLO, cod liver oil, 3 drams.

CASE 2.— R. C., a boy, aged 8 months, weighing 5.2 Kg., was admitted to the Milwaukee Children's Hospital, May 10, 1926, with the diagnosis of upper respiratory infection, rickets and infantile tetany. His temperature at admission was 103.8 F., and his serum calcium was 6.23 mg. per hundred cubic centimeters. Sixty units of parathyroid extract was administered on May 11 and on May 12. The amount of serum calcium was determined again on May 14, at which time the serum calcium was 6.29 mg., although the serum phosphorus had risen from 0.60 to 1.27 mg. per hundred cubic centimeters. During this time, the temperature had not dropped appreciably. On May 15 and again on May 16, forty-five additional units of parathyroid extract was given. On May 18, the serum calcium had risen to 8.44 mg., but during this time the temperature had dropped to 99.2 F., and the clinical evidence of both the tetany and the upper respiratory infection had disappeared. From May 18 to 24, calcium chloride was given orally in

doses of 10 grains (0.65 Gm.) three times daily, and throughout the stay in the hospital cod liver oil was administered. The serum calcium on May 24 was 9.38 mg. per hundred cubic centimeters. The rise in serum phosphorus from 0.60 mg. on May 10 to 2.85 mg. on May 24, although slower, in general paralleled the rise in serum calcium.

CASE 3.—F. S., a boy, aged 3 months, weighing 5.9 Kg., was admitted to the Presbyterian Hospital, Feb. 2, 1927, for feeding regulation. The temperature at admission was 99.4 F. The physical examination revealed that the infant was nervous, apparently free from clinical rickets and without clinical manifestations of infantile tetany. The day following admission, the infant's temperature rose to 103.2 F., and several watery stools were passed. At 2 o'clock the next morning, the infant had a severe convulsion with diaphragmatic spasm, which lasted for thirty minutes; during this convulsion, it was necessary to use mor-

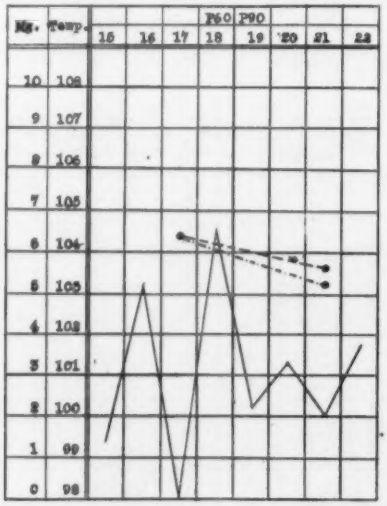

Chart 3 (case 3).—Data of administration of parathyroid extract. P 60 indicates parathyroid extract-Collip, 60 units.

phine and hot packs to release the spasm. The blood serum calcium at this time was 6.42 mg. per hundred cubic centimeters, and the serum phosphorus was 6.27 mg. A roentgenogram of the chest was negative for thymic enlargement. Sixty and ninety units, respectively, of parathyroid extract were given in divided doses of thirty units each on February 18 and 19. The determination of calcium made on the following day was 5.79 mg. per hundred cubic centimeters. During the interval that had elapsed since the convulsion, the infant was given chloral hydrate rectally to forestall any ensuing convulsions. In spite of this, on February 22, another severe convulsion developed, in which diaphragmatic spasm again predominated, although carpopedal spasm and a positive Chvostek's sign also were present. The child died in this convulsion. It will be noted from chart 3 that in this case the temperature remained high. The stools were still watery, although no focus of infection could be determined. Necropsy by Dr. Carl Apfelbach revealed a thymus measuring 8 by 5.5 by 0.7 cm.

and weighing 33 Gm. What part the thymus played in the clinical picture is not clear, although the predisposition of patients with thymic disease to sudden death is well known.

CASE 4.—E. K., a girl, aged 14 months, weighing 6.9 Kg., was admitted to the Presbyterian Hospital, March 9, 1927, with the diagnosis of upper respiratory infection, rickets and infantile tetany. The temperature at admission was 100.6 F., and the blood serum calcium was 5.78 mg. per hundred cubic centimeters. The temperature rose rapidly, and on the following day was 107.2 F. On March 11 and on March 12, ninety units of parathyroid extract was given in divided doses of thirty units. On March 12 an otitis media became apparent, and the right membrana tympani was incised. Frank pus was obtained, following which the temperature dropped rapidly to 101.6 F. on March 13; at this time the serum calcium was 7.0 mg. per hundred cubic centimeters, and the clinical signs of tetany were less marked. The temperature continued to drop

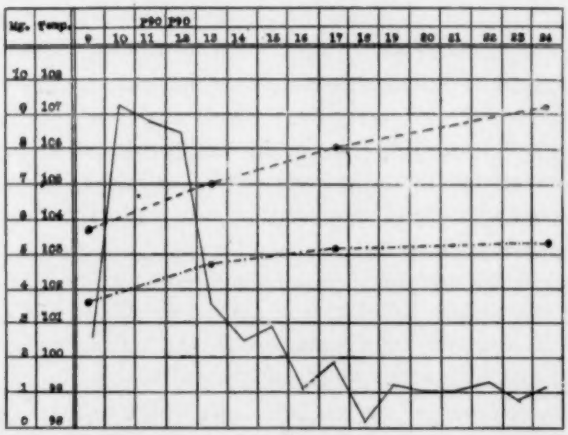

Chart 4 (case 4).—Data of administration of parathyroid extract. P 90 indicates parathyroid extract-Collip, 90 units.

gradually to normal. On March 17, the serum calcium was 8.0 mg. and on March 24, 9.1 mg. The rise in serum phosphorus was consistent with that of the calcium.

COMMENT

It is well known that infantile tetany is frequently precipitated by infection, and it is then logical to suppose that, with the recovery from the infection and the drop in the temperature to normal, recovery from the tetany and rise of the serum calcium and phosphorus values to normal should take place. That this actually does occur is suggested by the cases and charts in this paper. Just what part, if any, parathyroid extract played in the recovery of these cases, is not clear. Cases 1, 2 and 4 illustrate the rise in serum calcium and phosphorus simultaneous with the drop in temperature and the recovery from the infection without apparent relation to the administration of parathyroid

extract. Case 3 illustrates the failure of the serum calcium and phosphorus values to rise when parathyroid extract was administered, if recovery from the infection and drop in temperature failed to take place. It further suggests the fallacy of relying exclusively on parathyroid extract in the treatment of infantile tetany, without the aid of other well accepted means of raising the serum calcium and phosphorus values, such as cod liver oil and calcium by mouth and treatment with the quartz lamp. Just what part the thymic enlargement played in this case is not clear, although both convulsions that the infant suffered, the second of which resulted in death, were definitely of the tetanic spasm type and probably were not due to thymic enlargement. The enlargement of the thymus was then probably incidental and was not a factor in the clinical picture of tetany as presented.

SUMMARY AND CONCLUSIONS

1. Four cases of infantile tetany, in which parathyroid extract was used, are reported.

2. In cases 1, 2 and 4, the rise in serum calcium and phosphorus was definitely related to the recovery from infection, as evidenced by the drop in temperature, and apparently was not related to the treatment with parathyroid extract.

3. In case 3, the temperature remained high, and the serum calcium and phosphorus values failed to rise on administration of parathyroid extract. This case was complicated by thymic enlargement which was diagnosed at necropsy and was probably incidental.

4. The cases reported are too few from which to draw general conclusions as to the value of parathyroid extract in the treatment of infantile tetany.

5. It is unwise to rely on parathyroid extract to the exclusion of other better accepted methods of treatment in infantile tetany, until the parathyroid treatment is more firmly established on a sound clinical basis.

106 Monger Building.

SCARLET FEVER

IV. AMATO BODIES IN SCARLET FEVER *

JOHN A. TOOMEY, M.D.
AND
JOHN A. GAMMEL, M.D.
CLEVELAND

In 1913, Amato [1] described the bodies that have come to bear his name, ascribing to them a differential value in the diagnosis of scarlet fever. He found them in this disease from the first day of the invasion up to the second and third day of the desquamation, and represented them as small bodies—roundish, oval, elliptical, triangular, quadrangular or crescent shaped—in the cytoplasm of the ungranulated polymorphonuclear leukocytes, one or more of which appear in the leukocyte. These structures which stain with azur-blue are found either in the periphery of the leukocyte or near the nucleus, and are easily demonstrated in artificial light. Inside these Amato bodies, one may distinguish from one to four red or red-violet stained granules of different sizes, sometimes centrally and, if the Amato body is crescent shaped, peripherally placed. These red granules are barely visible and must be distinguished from the blue granules, which are sometimes found in the cytoplasm outside the Amato bodies. In some preparations, differentiation of the leukocyte is not clear, and in the cytoplasm finely punctate violet granules appear. In different methods of fixation, especially with fluids containing acetic acid, the neutrophilic granules may not be seen, but the granules of the Amato body hold fast to their color. In old slides in which the color fades, the neutrophilic granules may disappear, but the granules of the Amato bodies are still seen.

Amato found these bodies in all cases of scarlet fever, and thought that their number paralleled the severity of the disease. He at first considered them of such morphologic significance that he believed they

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* From the Division of Contagious Diseases, Cleveland City Hospital and the Department of Pediatrics, Western Reserve University.

1. Amato: A New Morphological Entity in the Blood of Scarlet Fever Patients, Lo Sperimentale **67**:45, 1913; Later Research on the Blood in Scarlet Fever, ibid. **75**:383, 1921.

were organisms, probably protozoa. Tron [2] found these inclusions in thirty-six of the forty cases studied, and stated that they were especially abundant at the beginning of the rash; that they were absent in the complications of scarlet fever, and that they reappeared in recurrent scarlet fever and disappeared with recovery. Tron and Amato looked for these bodies in various diseases—pneumonia, measles, pertussis, dysentery, mumps, erysipelas, varicella, rabies, empyema, staphylococcic infections, dermatitis, serum exanthem and toxin exanthem—with negative results. The blood cells of normal persons working in the scarlet fever ward were normal. Salembeni [3] described an organism in the cytoplasm of the leukocytes of scarlet fever which Amato believes is similar to his body. Pauli [4] considered that Amato bodies are found only in patients with scarlet fever, while Cartia and Rapisardi [5] found them in other patients and only in 51.4 per cent of the cases of scarlet fever examined. Both Amato and Tron lay great stress on the differentiation of their inclusion bodies from those described by Döehle, the former believing that the Amato bodies are specific entities not easily produced in animals, as are Döehle bodies, and that they are found in the cells of patients who have died from scarlet fever. Another differentiating point is that the Amato bodies take a lighter staining of blue for the background of the red granules, which constitute the most distinctive feature. In many of the slides, we were able to see Döehle bodies and Amato bodies in the same leukocyte, the only difference being that an occasional granule might be present in the blue inclusion field of the leukocyte, making it, according to the authors, an Amato body. Because of the frequency with which the Döehle bodies are present in the same leukocyte, and because of the ever present granular leukocytic degeneration in the leukocytes of patients having scarlet fever, we do not see how such fine differentiation can be considered reasonable; Amato bodies are nothing else than Döehle bodies with an occasional red granule present, the former being present more frequently.

In this clinic, we have studied 100 cases—50 controls, and 50 cases of typical scarlet fever. After various experimentation, we have found

2. Tron: A Report on Finding Amato Bodies in the Blood of Scarlet Fever Patients, Lo Sperimentale **76**:31, 1923; abstr. in Zentralbl. f. d. ges. Kind. **15**:34, 1923.

3. Salembeni: Compt. rend. Acad. d. sc., 1914; quoted by Amato (footnote 1).

4. Pauli: The Leukocyte Inclusions in Scarlet Fever, Lo Sperimentale **78**: 143, 1924.

5. Cartia and Rapisardi: Later Observations on Leukocyte Inclusions in Infectious Diseases, Pediatria **33**:576, 1925.

that it is necessary to conform strictly to the technic described by Amato in order to get good results.

Technic of Amato.—Clean a cover slip, free it of soap, and dry it in the air; take the blood smear and let it dry in the air; fix the slide in alcohol (absolute) for ten or fifteen minutes, and again dry in the air, stain for three or four hours with the special solution as described below, using the microscope as a control for the staining if necessary. When staining, the slides are put on two glass rods or toothpicks with the film side down; when the slides are taken from the staining solution, they should be quickly rinsed with distilled water, decolorized in absolute alcohol if overstained, dried in the air and examined with a high power lens only.

Solution for Staining.—A solution consisting of 2 cc. azur 2 (watery solution, 0.8: 1,000) and a solution consisting of 25 cc. eosin solution, 1: 20,000, were used. Both solutions are mixed immediately before use, and can be used only once. Ocular 10, oil immersion, 1/12, and the tent house type of artificial light were used, with blue-white ground glass slide, for even light transmission.

Only typical cases of scarlet fever were taken, i. e., cases showing good rashes, and only well stained slides were studied. Two hundred leukocytes were counted in each instance except in the two cases of so-called surgical scarlet fever, in which 400 cells were counted. When

TABLE 1.—*Reactions in Fifty Cases of Scarlet Fever*

		Positive	Doubtful	Negative
Adults	13	11	None	2
Children	37	28	3	6
Per cent positive	..	78	6	16

the rash was present, the clinical diagnosis definite, and the slides negative when 200 leukocytes had been counted, 200 additional leukocytes were studied. Table 1 indicates the reactions in the fifty cases of scarlet fever.

Of these fifty patients, five died, four having had inclusion bodies. Two of the three patients having postpartum scarlet fever died, both having had numerous inclusion bodies. There were two cases of surgical scarlet fever, one presenting all the symptoms of scarlet fever. This was the case in the positive group, in which we saw the greatest number of inclusion bodies. The other showed a typical rash, but no sore throat or glandular enlargement, and no inclusion bodies. If we consider the cases that presented typical scarlet fever and that did not show inclusion bodies, we find one case of surgical scarlet fever, another case occurring in the postpartum period and six cases of typical scarlet fever in each of which the rash was blanched by the serums from patients convalescing from scarlet fever. Three of the patients had an extremely mild type of the disease, and the presence of Amato bodies was doubtful.

In the control series, nine of the fifty patients examined had Amato bodies present in the blood. These nine positive control cases included two cases of measles, three of diphtheria, one of tuberculous pneumonia, one of stricture fever, one of pneumonia, and one of epidemic meningitis, the latter presenting the most Amato bodies seen in either the positive or the negative group.

CONCLUSIONS

Amato bodies are not always found in scarlet fever and are found in other diseases, although they are present more commonly in scarlet fever than in any other acute infection.

A STUDY OF THE ANTIRACHITIC FACTOR IN HUMAN AND IN COW'S MILK*

ALFRED F. HESS, M.D.
AND
MILDRED WEINSTOCK, B.S.
NEW YORK

Rickets is a universal disorder. It occurs with by far the greatest frequency among infants and young children in the temperate zones, but no country seems to be spared and no climate to confer absolute immunity. In considering and in studying this widespread disorder, one should always bear in mind that milk is the universal food of infants; whatever may be the differences as to detail, the basic diet of every infant is either woman's milk or that of some animal. It is therefore of prime importance, in studying the etiology of rickets, to have as complete an understanding as possible of the relation of woman's and of cow's milk and their constituents to the development and prevention of rickets. Strangely enough, no experimental study has been undertaken of human milk in its bearing on rickets, so that it seemed worth while to investigate this problem, making use of the methods which recently have been evolved in the laboratory.

There is a fundamental difference between the relation of milk to rickets and its relation to some of the other nutritional disorders of infancy which are commonly grouped with rickets, for example, infantile scurvy. Susceptibility to scurvy bears an inverse rather than a direct ratio to the quantity of milk consumed. In other words, if milk is of average antiscorbutic potency, the chance of developing scurvy will be far greater if the dietary has included a small rather than a large daily quota. The same is true of xerophthalmia, which comes about from a lack of vitamin A, and of infantile beri beri, which is thought to be due to a lack of the antineuritic vitamin. In regard to rickets, the situation is the opposite—instead of susceptibility being in inverse ratio to the consumption of milk, it is rather in direct ratio; for example, if an infant, aged 6 months, is given a pint of milk a day, it is less apt to develop rickets than if it consumes a quart a day. It is evident that from a nutritional standpoint there must be an essential etiologic difference between rickets and these other disturbances, and that they all cannot be ascribed to the deficiency of a specific vitamin in the milk.

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*From the Department of Pathology, College of Physicians and Surgeons, Columbia University.

*Read before the American Pediatric Society, Niagara Falls, June 1, 1926.

One important point must be constantly borne in mind in all studies of rickets that are based on animal tests. As is well known, the animals commonly used for these investigations are the rat and the dog, especially the former. It is highly essential, therefore, to remember that the reaction of the rat toward the content of phosphorus and calcium in the diet is different from that of the infant. Either or both of these chemical constituents may be added ad libitum to the dietary of the infant without preventing or curing rickets, whereas if they are supplied in proper ratio in the dietary of the rat, rickets regularly will be prevented or cured. In other words, the rat is able to absorb and utilize the calcium or phosphorus in the food, whereas the infant is unable to take advantage of these salts unless the antirachitic factor is supplied or other conditions are favorable. It is not known whether a similar distinction exists between the dog and the infant in regard to their response to the phosphorus and calcium of the dietary.

Although there is no unanimity of opinion as to what foods should be regarded as rachitogenic and more particularly as to the degree to which any of them tends to produce rickets, all are agreed that in the prevention of this disorder human milk stands preeminent. The incidence of rickets among infants fed on human milk is everywhere decidedly less than that of those brought up on cow's milk. Some years ago, we found that whereas approximately all bottle-fed infants in New York City showed signs of rickets by March, unless they had received specific therapy, only from one third to one half of the breast-fed infants manifested signs at this seasonal peak. The purpose of the present study was to ascertain, if possible, the nutritional factors which were responsible for this marked difference in reaction, at any rate, to determine whether this distinction was due to a comparative superiority of human milk in the antirachitic factor.

It seems unnecessary to review in detail the technic of our investigation, as it was similar to that employed in other experiments on rickets, the reports of which have been published from this laboratory during the past five years or more. In other words, rats, aged 4 weeks, have served as the test animals, and the standard test dietary has been the low phosphorus Sherman-Pappenheimer ration, which is fed for periods of four weeks before roentgenograms are made and the animals are killed. The results with cow's milk may be summarized by the statement that when from 20 to 25 cc. were added to the standard ration, the development of rickets was prevented. The blood of animals receiving a supplement of 20 cc. of this milk daily contained about 5 mg. per cent of inorganic phosphorus. On the other hand, when human milk was added in the same amount, namely, from 20 to 25 cc. daily, it did not exert any appreciable protective influence; the animals

all developed rickets in moderate or even marked intensity, and their blood contained a low percentage of phosphorus, only 1.5 mg. per cent (table 1). From the standpoint of rickets, it seemed hardly to have improved the standard diet for producing rickets. It was found that from 25 to 30 cc. of human milk had to be added to this ration to confer protection. The fat content of this milk, as of the cow's milk, was approximately 4 per cent. We are therefore face to face with conditions that are just the opposite of those which prevail in the feeding of infants—whereas human milk is definitely superior in preventing infantile rickets, it is definitely inferior in preventing the development of rickets in rats. This paradoxic result is due in part to the factor that has been referred to, namely, the comparatively high percentage of phosphorus in cow's milk, which contains about three and

TABLE 1.—*Comparative Antirachitic Value of Human and of Cow's Milk*

Weight of Rats (Gm.)	Rickets-Producing Diet	Supplement to Diet	Rickets (Microscope)	Blood Phosphorus (Inorganic)
40-70	Low phosphorus no. 84	14 cc. human milk	Marked	
42-74			Marked	
34-60			Marked	1.63 mg.
40-64			Marked	
40-80		14 cc. cow's milk (raw)	Very slight	
48-100	Low phosphorus		Very slight	
38-94			No	2.8 mg.
40-96			No	
34-40		20 cc. human milk (raw)	Marked	
60-70	Low phosphorus		Moderate	1.35 mg.
50-80			Moderate	
30-80		20 cc. cow's milk (raw)	Very slight	
40-84	Low phosphorus		No	5.02 mg.
62-124			No	4.65 mg.
42-50		Control	Marked	
40-45	Low phosphorus		Marked	1.47 mg.
40-50			Marked	
50-54			Moderate	

one-half times as much phosphorus as human milk. As stated, although this difference in phosphorus content is of little moment in connection with the development of rickets in infants, it is highly significant in relation to the rickets of rats. An experiment of this kind indicates first that the antirachitic value of cow's milk is greater for rats than that of human milk, and, second, as emphasized in the abstract of this paper,[1] *human milk contains only a small amount of the antirachitic factor.* Otherwise, human milk would have prevented the development of rickets, for the specific factor, frequently termed "vitamin D" or the "antirachitic vitamin," exerts its protective power on rats as effectively as on infants. In fact the rat is the standard test animal for assaying the potency of antirachitic substances, such as cod liver oil and egg yolk. It would seem, therefore, that *the high protective value*

1. Hess, A. F., and Weinstock, M.: Abstr., Am. J. Dis. Child. **32**:458 (Sept.) 1926.

of human milk in infantile rickets cannot be ascribed to its content of the antirachitic factor.

It must be admitted that there is no knowledge as to the constituents of human milk which are responsible for its marked antirachitic potency. Possibly this character is due to the favorable equilibrium of the various ions that it contains, resulting in conditions which greatly further absorption and retention of calcium and phosphorus. This hypothesis is attractive but highly speculative, for as yet physicians are just as much in the dark in regard to the pathogenesis of rickets as they were in the preexperimental era. There is, however, one aspect of this question, although not perhaps a major factor, which seems worth bearing in mind. One of the distinctive characteristics of human milk is its exceptionally high content of lactose, of which it contains from 6 to 7 per cent compared to the 4 per cent in cow's milk. As Bergeim [2] recently has demonstrated, the ingestion of lactose tends to bring about an acid reaction in the intestinal tract which favors the absorption of calcium. Other sugars do not have this effect. Some years ago, Zucker [3] found that the urinary calcium in man could be increased by the addition of acid to the diet, a phenomenon that he interpreted as indicating greater absorption. It seems therefore pertinent to raise the question whether the lactose of human milk does not induce a reaction of the chyle, which is comparatively favorable for the calcium and phosphorus balance.

EXPERIMENTS WITH CREAM

In another series of experiments, the question was approached from a different angle. An attempt was made to concentrate the antirachitic component of cow's milk into one of its fractions, especially into the fat. It may be stated at the outset that the cow's milk used in this entire investigation was raw and certified and was produced by a herd that was stall-fed and received a standardized ration, which included about 35 pounds of ensilage per capita daily. Although the hygienic conditions were of the best, the cows were out of doors for only a short period every day and received little sunlight. Attention was focused more particularly on the cream of the milk, in view of the fact that the specific nutritional factor is fat soluble. It was found that an addition daily of 6 cc. of cream to the standard dietary brought about almost complete protection, which was rendered complete when 8 cc. was added. A record of this experiment may be seen in table 2. It cannot be inferred that the antirachitic value of the cream depended on its content of phosphorus, for, as recently ascertained in analyses carried out in this laboratory,[4] cream contains a less percentage of

2. Bergeim, O.: J. Biol. Chem. **70**:35 (Sept.) 1926.
3. Zucker, T. F.: Proc. Soc. Exper. Biol. & Med. **18**:272, 1921.
4. Hess, A. F., and Helman, F. D.: J. Biol. Chem. **64**:781 (July) 1925.

phosphorus than does whole milk. Nor can the antirachitic value of cream be attributed to a greater percentage of lipoids, such as lecithin and cholesterol, for it has been definitely established that these lipoids do not posses any antirachitic property. It would seem that its protective quality is to be ascribed rather to a specific nutritional factor. As is well known, vitamin A as well as the antirachitic factor is active in the calcification of bone. Vitamin A is peculiarly sensitive to

TABLE 2.—*Antirachitic Value of the Fat in Cow's Milk*

Weight of Rats (Gm.)	Rickets-Producing Diet	Supplement to Diet	Rickets	
			Macroscopic Silver stain	Microscopic
35-40	Low phosphorus no. 84	12 cc. whole milk	Moderate	Moderate
46-100			Moderate	Moderate
54-102			Moderate	Moderate
35-84			Moderate	Moderate
30-70	Low phosphorus	6 cc. upper third milk*	Moderate	Moderate
40-82			Moderate	Moderate
50-84			Marked	Marked
54-106	Low phosphours	12 cc. upper third milk	Moderate	Moderate
34-80			Moderate	Moderate
54-84			Moderate	Moderate
40-66			Very slight	No
60-60	ow phosphorus	6 cc. cream (20 per cent)	Very slight	No
30-50			Very slight	No
28-50			Slight	Slight
40-70			Slight	Slight
30-44	Low phosphorus	8 cc. cream (20 per cent)	No	No
36-60			No	No
40-52			No	No
40-60			No	No
50-50	Low phosphorus		Marked	Marked
42-60			Marked	Marked

* Upper 10 ounces of milk from quart bottle.

TABLE 3.—*Comparison of Oxidized and Nonoxidized Cream*

Weight of Rats (Gm.)	Rickets-Producing Diet	Supplement to Diet	Rickets		Blood Phosphorus (Inorganic)
			Roentgenographic	Microscopic	
30-50	Low phosphorus no. 84	8 cc. cream (20 per cent) oxidized	No	No	
42-60			No	No	
36-52			No	No	5.95 mg.
32-54			No	No	
30-44	Low phosphorus	8 cc. cream (20 per cent)	No	No	
36-60			No	No	4.60 mg.
40-52			No	No	
40-60			No	No	
30-28	Low phosphorus	Control	Moderate	Moderate	
38-36			Moderate	Moderate	
30-30			Moderate	Moderate	
40-36			Slight	Moderate	

oxidation and can be destroyed readily in this way. In order to ascertain the rôle of vitamin A in our experiment, tests were carried out in which 8 cc. of oxidized cream was added to the dietary. This cream, which likewise contained 20 per cent of fat, was subjected for twenty-four hours to a current of air which had been warmed to 45 C. As will be noted in table 3, the addition of oxidized cream prevented the development of rickets as effectively as ordinary cream; rickets was

absent, as judged by the roentgenographic picture, the content of phosphorus in the blood and the microscopic examination of the epiphyses. It is evident, therefore, that vitamin A did not play the significant rôle in the protection brought about by the cream.

EXPERIMENTS WITH UPPER-THIRD MILK

Parallel with this experiment, a series of tests was undertaken in which "upper-third milk" was added instead of 20 per cent cream. By the term "upper-third milk" is meant the upper 10 ounces removed from a quart bottle of milk. This upper layer, when obtained from milk with a content of 4 per cent fat, contains, as has been shown by many investigators, approximately 10 per cent of fat. "Upper-third milk" was tested in view of the fact that it has been frequently used in the preparation of mixtures for infant feeding. Twelve cubic centimeters of this 10 per cent milk was given as the equivalent of the 6 cc. of 20 per cent cream which had been tested in the previous experiments. It will be noted in table 2 that 12 cc. of "upper-third milk" conferred little protection on the experimental animals, and that in this respect its activity was not comparable to that of an equivalent amount of cream. These results suggest that there is a rachitogenic factor in milk which is present in the skimmed fraction and which, when given in addition to the cream, offsets to a certain degree its rickets-protective properties. This series of experiments would indicate that 20 per cent cream has sufficient antirachitic potency to be considered in connection with the prevention of rickets in infants.

As was to be expected, the casein fraction of the milk did not manifest any antirachitic potency. When 2 per cent of casein was added either to cow's milk or to human milk, rickets developed in undiminished degree. We were unable to determine whether the disorder was increased by this supplement. In this connection, it may be mentioned that several years ago we found that egg white added to the standard ration intensified the degree of rickets. That casein does not possess any antirachitic potency may be inferred from the fact that it is almost impossible to protect rats from rickets by means of a supplement of skimmed milk, in which the percentage of casein is undiminished; a few animals were induced to consume as much as 100 cc. per capita daily and were protected by its high phosphorus content. Lesser amounts were ineffective in this respect.

It is evident that from a dietetic point of view the antirachitic value in the cream of cow's milk is so slight as to be negligible. The small amount of antirachitic factor which is associated with the fat of the milk is more than counterbalanced by the constituents in the remaining portion, so that cow's milk must be regarded as an infant's food—productive of, rather than protective from, rickets. No doubt it may acquire some rachitic value by subjecting the cow to ultraviolet rays

or by giving a fodder of high antirachitic potency. We shall not discuss in detail the possibility of increasing the antirachitic titer by irradiation of the animal, as this question was considered in a recent paper on the "Antirachitic Properties Developed in Human Milk by Irradiating the Mother."[5] The subject may be summarized by the statement that although it is possible to develop antirachitic qualities in the milk of probably all animals by intense irradiation from artificial sources, such as the mercury vapor lamp, solar irradiation exerts comparatively little effect in this respect. Moreover, even the milk secreted by an animal which has been irradiated with the mercury vapor lamp is much weaker in antirachitic factor than milk which has been subjected directly to these radiations. According to our experience and to that of some others, irradiated dried milk, when fed to infants in the customary amounts, is as potent an antirachitic as cod liver oil. On the other hand, although solar irradiation of the cow produces slight antirachitic potency in the milk, as judged by delicate laboratory tests, this measure is of doubtful importance clinically. Five years ago this problem was investigated by a prolonged observation of two groups of infants—the one given milk obtained from stall-fed cows ("winter milk") and the other group, milk from pasture-fed cows ("summer milk").[6] At the end of the winter it was found that, as judged by roentgenograms, approximately an equal number of the infants had developed rickets. Some years ago a similar result was obtained in regard to the effect of sunlight on vegetables—for example lettuce, which had been grown out of doors exposed to the July sun, had acquired almost no antirachitic value. Tropical sunlight is different in this respect, as indicated by its power to activate the copra from which coconut oil is prepared. It is possible, therefore, that in the tropics cow's milk possesses greater antirachitic value and that infants fed on this milk benefit appreciably. In this connection, it should be mentioned that the milk used for all of our tests was obtained during the winter season, for the most part during January and February.

Attempts have been made to render milk of protective value by feeding cod liver oil to animals. This is an aspect which has been considered in several papers that have emanated from this laboratory.[7]

5. Hess, A. F.; Weinstock, Mildred, and Sherman, E.: Antirachitic Properties Developed in Human Milk by Irradiating Mother, J. A. M. A. **88**:24 (Jan. 1) 1927.

6. Hess, A. F., and Unger, L. E.: Seasonal Variation of Rickets, Am. J. Dis. Child. **22**:186 (Aug.) 1921.

7. Hess, A. F., and Weinstock, Mildred: Proc. Soc. Exper. Biol. and Med. **20**:371, 1923; Antirachitic Effect of Cod Liver Oil Fed During Period of Pregnancy or Lactation, Am. J. Dis. Child. **27**:1 (Jan.) 1924; Rickets as Influenced by Diet of Mother During Pregnancy and Lactation J. A. M. A. **83**:1558 (Nov. 15) 1924.

In the first, published in 1924, we came to the conclusion that "the active principle of the oil is not excreted in adequate amount" in the milk, and in a later paper, which viewed the question from a clinical standpoint, that by this means "rickets cannot be prevented . . . although it can be mitigated to a certain degree." These results have been confirmed in a recent paper by McCollum and his co-workers.[8] From all that has been published, it is evident that little will be accomplished clinically by this means and that one cannot hope to prevent the occurrence of rickets by supplying the cow with a fodder rich in the antirachitic factor.

In view of the fact that infants develop rickets not infrequently even on the normal diet of human milk, one would expect that nature might have provided numerous other sources of this specific nutritional factor which might serve as supplements to the dietary. In point of fact, just the contrary is true; of all the vitamins, none is so poorly distributed among foods as the antirachitic factor. As is well known, it is entirely absent in the cereals and in fruits. Some years ago, when a distinction had not been drawn between the antirachitic factor and the fat-soluble vitamin, it was thought that vegetables, more particularly the leafy vegetables, were of protective value in rickets. Such, however, is not the case. In 1920, Hess and Unger [9] reported the incidence of severe rickets in an infant which had received daily, for a long period, a diet containing a liter of milk and 30 Gm. of spinach. Zucker and Barnett [10] showed that even the concentrated (nonsaponifiable) extract of spinach was devoid of the factor that protects from rickets. More recently Chick and Roscoe,[11] in a paper that may be consulted for the complete literature of this subject, reported that "spinach grown in the open in winter, spring or autumn possesses no antirachitic properties and that spinach grown in mid-summer has a slight but appreciable antirachitic value." From a clinical standpoint, its potency in this respect is negligible.

It has been shown over and over again that the fish oils, especially those prepared from the liver, contain this factor in greatest concentration—the oil from the puffer fish, the cod and the herring. Whether one should consider fish oil a food or a therapeutic agent is a question of definition; if a food, it must be regarded as an uncommon one. By far the most available source of this factor among the every day foods is the egg, the yolk of which contains it in marked concentration.

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8. McCollum, E. V.; Simmond, N.; Becker, J. E., and Shipley, P. G.: Studies on Experimental Rickets, Am. J. Dis. Child. **33**:230 (Feb.) 1927.

9. Hess, A. F., and Unger, L. E.: Clinical Rôle of Fat Soluble Vitamin, J. A. M. A. **74**:217 (Jan. 24) 1920.

10. Zucker, T. F., and Barnett, M.: Proc. Soc. Exp. Biol. and Med. **29**: 375, 1923.

11. Chick, H., and Roscoe, M. H.: Biochem. J. **20**:137, 1926.

For this reason egg yolk has a particular value in the dietary of the infant and, it may be added, of the nursing mother. Chicken liver and chicken fat have a high protective value, both the fat from the subcutaneous tissues as well as that from the region of the gizzard. In some experiments carried out with these fats it was found that they are even more potent than the liver. One fourth of a cubic centimeter daily of either of these fats and 0.5 Gm. of chicken liver protected rats which had been placed on the ration that would produce rickets. It may be added that 0.5 Gm. of ovary failed to ward off rickets.

Butter has a slight value, but insufficient to be depended on to protect against rickets. We have frequently observed rickets develop in infants who were receiving 5 Gm. of butter added to the milk mixtures. The same is true of beef drippings, a preparation that is used largely in England. Several years ago drippings of beef fat were fed daily in 30 cc. amounts to a series of infants but failed to prevent the development of rickets. Beef marrow is of some value; Bosányi [12] has shown experimentally the potency of this tissue.

It is evident, therefore, that the antirachitic factor is sparsely rather than generously distributed in nature. From a clinical point of view it should be thought of as existing in eggs, in liver and to a lesser extent in some of the animal fats. Viewed broadly, the position of rickets in relation to antirachitic foods is difficult to understand. A pathologic condition is developing in infants in spite of the fact that they are fed on a natural food—human milk—and are living under conditions which are regarded as normal. From the standpoint of physiology, such a phenomenon is clearly illogical. We can attempt to extricate ourselves from this position by concluding that the mild degree of rickets which develops in breast-fed infants should be regarded as a physiologic rather than as a pathologic variation. It would seem, however, that this view is not reasonable, as it necessitates the presumption of two physiologic conditions presenting divergent histologic pictures. A more natural deduction would seem to be that even the nursing infant is not completely adjusted to living conditions in the temperate zones, and that rickets is its pathologic reaction when deprived of the solar irradiation which is an essential complement to its diet. A corollary of these observations is the conclusion that rickets cannot be regarded as a disorder caused by a deficiency of vitamin, since ideal food for the infant—human milk—is exceedingly poor in the antirachitic factor; and, furthermore, the more of this food it receives, the greater is the tendency for rickets to develop.

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12. Bosányi, A.: Experimental Studies on Rickets, Am. J. Dis. Child. **30:** 780 (Dec.) 1925.

THE SPLEEN IN MEASLES*

EMANUEL FRIEDMAN, M.D.
DENVER

In the course of an epidemic of measles during the winter of 1922, Bleyer of St. Louis had 264 patients under his care. These included children seen at institutions and in private practice. The epidemic was considered mild in character. All the children observed were under 12 years of age, and the majority under 7.

Bleyer made the unexpected discovery that with the onset of the eruption, the spleen became abruptly enlarged and that this enlargement just as promptly receded with the disappearance of the rash. On the day preceding the eruption, only 2 per cent of the spleens were palpable, and this figure mounted to 24 per cent on the first day of the rash and to 43 per cent on the second day, reaching the peak on the third and fourth days when the incidence of enlargement was 56 and 52 per cent, respectively. On the fifth and sixth days, which marked the decline of the rash, the proportion showing enlargement decreased to 25 per cent, and the extent of enlargement was reduced to about half. During the period of convalescence, hypertrophy was still manifest in 15 per cent of the cases.

During the height of the eruption, the spleen could be felt for a distance of from 1 to 3 cm. below the costal arch. The enlargement was in no way influenced by the severity of the infection nor by the supervention of such complications as otitis, pneumonia or sepsis.

These observations were confirmed during the following two winters when an additional group of 133 cases of measles was carefully studied.

The author was struck by the unusual nature of his observation. Reference to the standard textbooks on pediatrics, medicine and pathology developed the fact that most authorities did not mention the spleen in connection with measles; and the few references encountered were to the effect that the spleen is not palpable in the course of measles. In all the clinical textbooks consulted, Osler and McCrae alone spoke of a slight enlargement usually being found.

On the strength of his observation, Bleyer makes the plea that enlargement of the spleen be included in the symptom-complex of measles. His publication [1] was the subject of extensive and favorable editorial comment.[2]

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* Received for publication, June 20, 1927.

1. Bleyer, Adrien: Enlargement of the Spleen in Measles, Am. J. Dis. Child. **31**:26 (Jan.) 1926.

2. The Spleen in Measles: An Overlooked Symptom, Editorial, J. A. M. A. **86**:1217 (April 17) 1926.

When the article in question claimed my attention, it aroused more than ordinary interest. I found it difficult to reconcile the inconspicuous rôle of the spleen in measles as reflected in standard textbooks with the high incidence recorded by the author. My own impression was that this organ was not enlarged in rubeola. I was prepared to concede that it was easy enough to overlook a slight enlargement, but when this reached 3 cm. below the costal arch, its detection should present no difficulty. I therefore eagerly awaited a chance to confirm or refute the observation of the St. Louis clinician.

The opportunity presented itself during the winter of 1927, when Denver and its vicinity experienced a protracted and severe epidemic of measles, which lasted about four months and attacked upward of 7,000 children.

I made a careful palpatory investigation of the spleen in each case under my care. In many, a decision was reached only after prolonged and repeated examination. Considerably more time was devoted to ascertain the presence or absence of enlargement than is possible under ordinary circumstances.

In the course of the epidemic, I observed 118 cases of measles. Two were excluded from consideration because of preexisting splenomegaly, leaving 116 cases on which my study is based. This number, while considerably smaller than that of Bleyer, is nevertheless sufficiently large for valid deductions to be made.

The first case encountered was in the latter part of November, 1926; only three were seen in December; the majority occurred during the three succeeding months, and only nine in April.

Sixty-one of the patients were male, and fifty-four, female. I had not seen any child under 6 months of age; three were under 1 year; thirty-five, between the ages of 1 and 5 years; seventy-four between 5 and 10 years; three between 10 and 11, and one between 14 and 15.

The epidemic was considered moderately severe, as judged by the degree of prostration, the height of the temperature curve, and the frequency and severity of complications.

Because all my patients were seen in private practice, I could not visit them as often as I should have for the purpose of critical study without appearing importunate. Four were seen only during the pre-eruptive stage; a group of eighty-nine, during the height of the eruption as well as during other stages and thirteen only, during the stage of decline.

Of the 116 cases, only 14 showed a palpable spleen and of these, 4 disclosed only slight enlargement. In 6, the enlargement was of moderate degree, and in only 1 case was it considered striking. The average age of the group showing slight enlargement was 6 years, and of the group with moderate enlargement, 3 years.

All but one of the patients who showed splenic enlargement were males.

In the series, thirteen patients were classed as having had a severe attack of measles—five with bronchopneumonia, and one with sepsis. It is noteworthy that not one of these presented an enlarged spleen.

Of the fourteen children with a palpable spleen, seven were seen only once; three at the commencement of eruption, and four when the efflorescence was well advanced. The degree of enlargement was approximately the same in the two groups. In one instance, the enlargement was present during the beginning of eruption and had disappeared during its height. In four, I failed to note enlargement at the beginning, whereas it was present during the height of the exanthem. In one case, the enlargement was present both at the beginning and at the height of the eruption, and was of equal extent. In one case, the enlargement was detected only during the stage of defervescence. I could not note any difference in the degree of enlargement in any child, when examined on several occasions, to correspond to the different stages of the eruption.

SUMMARY

In 116 cases of measles, enlargement of the spleen was found in fourteen, or 12 per cent. In four cases, this enlargement was so slight as to have easily escaped detection under ordinary circumstances.

Hypertrophy was present in only one female.

Not one of the more seriously sick children nor of those with the ordinary complications showed an enlarged spleen.

The enlargement was more pronounced in the younger children.

The degree of enlargement was independent of the stage of eruption.

The frequency of enlarged spleens was almost as great during the early stage as during the height of the eruption.

CONCLUSIONS

This study confirms the observations of Bleyer that splenic enlargement occurs in measles and that this enlargement is not dependent on existing complications nor is it commensurate with the severity of the infection.

However, the incidence of splenomegaly in my smaller series is less than one-fourth that noted by Bleyer.

The conclusion appears warranted that an enlarged spleen is not a prominent nor a frequent occurrence in measles at any stage of its development.

326 Republic Building.

SPONTANEOUS AND INDUCED KETOSIS IN CHILDREN

EFFECT ON THE GLUCOSE TOLERANCE TEST *

JEROME L. KOHN, M.D.

MARGARET E. FRIES, M.D.

AND

GERTRUDE FELSHIN, M.D.

NEW YORK

The effect of ketosis on carbohydrate metabolism has been studied by the use of the glucose tolerance tests. Many have studied the immediate results of ketosis, but few have considered the period following it. To ascertain this after-effect, it was necessary to study the two preceding periods; first, before the onset of ketosis; second, during the ketosis.

Two groups of children were investigated; first, children who developed ketosis on a ketogenic diet; second, children who were admitted to the hospital in a state of ketosis following cyclic vomiting. It is difficult to say whether the two forms of ketosis are comparable; certainly, the etiologic factors are so different that we considered it best to study them separately.

The first group consisted of nine children, six boys and three girls, ranging in age from 6 to 12 years. Eight of these patients were admitted to the pediatric service of Mount Sinai Hospital because of chorea, and one (number 9), was admitted because of frequent convulsive seizures, not a result of idiopathic epilepsy. All these patients were first treated in the usual manner, i. e., by rest in bed and a well proportioned diet. The ketogenic diet was then begun and continued for a period; this was followed by another period of a well balanced diet.

The influence, if any, of a ketogenic diet on chorea was deducted from the clinical progress of the case. Ketosis induced by prolonged starvation or by a high fat diet has a quieting effect on the central nervous system. This fact has been made use of in the treatment of epilepsy; convulsive seizures can be materially lessened during ketosis. It was thought that perhaps a similar ketosis would have a quieting effect on children with chorea, but this was not the case.

The first period when the child was at rest and on a well balanced diet, served as a control period for the study of the sugar tolerance.

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* From the Department of Pediatrics, Mount Sinai Hospital.

The tolerance was then again determined during ketosis and once more following the cessation of the ketosis.

The test was begun after an overnight fast of fourteen hours. The children were kept in bed during their entire stay in the hospital. In the first few cases, Epstein's modification of the Benedict microchemical method for blood sugar was used; in the remainder a micromodification of the Folin-Wu method. Two tenths of a cubic centimeter (0.2 cc.) of blood was obtained by pricking the finger. Samples of blood were taken previous to the ingestion of glucose, thereafter every half hour for two hours and a final sample after three hours, making six tests in all. Other food or water was not permitted until the completion of the test. The specimens were analyzed the same afternoon by one of us. Specimens of urine were collected, when possible, at half hour intervals for four hours.

The amount of glucose given was estimated in relation to the children's sitting height squared; i. e., 0.0085 Gm. of glucose per square centimeter of the sitting height squared. If correlated with the weight of the child, it averaged from 1.4 to 1.7 Gm. of glucose per kilogram of body weight. From previous tests on 100 normal children, Fries and Kohn [1] found the sitting height more satisfactory than the weight, since the sitting height is in relation to the expected weight and to the surface area. The surface area is a more accurate basis for calculation in overweight and underweight children. For children of normal weight and stature, either method may be used as a basis for the amount of glucose to be given.

The glucose was given in a 30 per cent solution, to which was added a little lemon juice to make it more palatable. Chemically pure anhydrous glucose was used, the water being added just before ingestion.

None of these children had a severe chorea; patient 4 alone had fever during the period of observation in the hospital. This fever appeared during the postketosis period. The children were kept in bed and on a prescribed diet, fixed as to caloric value. The diet consisted of about 60 per cent carbohydrate, 15 per cent protein and 25 per cent fat.

The blood sugar curve during the control period, i. e., while the children were on a well proportioned diet, was similar to those found by Fries and Kohn [1] in 100 normal children; i. e., the fasting blood sugar varied from 80 to 100 mg. per hundred cubic centimeters of blood; the maximum rise occurred within the first hour after glucose ingestion and ranged from 140 to 180 mg. The blood sugar returned to its

1. Fries, M. E., and Kohn, J. L.: Glucose Tolerance Tests in Children, Am. J. M. Sc. **170**:547 (Oct.) 1925.

original level within three hours (chart 2, curve 1 and 2). When possible, two control tests on two different days were performed.

The diet was then changed from a mixed to a mild ketogenic one. The fatty acid-glucose ratio of the diet was calculated from the Woodyatt [2] formula:

$$\frac{\text{Fatty Acid}}{\text{Glucose}} = \frac{0.46\ \text{Protein} + 0.9\ \text{Fat}}{\text{Carbohydrate} + 0.58\ \text{Protein} + 0.1\ \text{Fat}}$$

At first, a fatty acid-glucose ratio of a diet calculated to be 2.5:1 was used. If acetone did not appear in the urine on this diet within two days, the ratio was increased to 3:1, and, when necessary, it was still further increased. The acetone in the urine was determined by the nitroprusside test. The glucose tolerance tests were usually done from three to five days after the beginning of the ketogenic diet; in case 12, the test was done on the first day after the ketogenic diet was started and was repeated a few days later.

RESULTS

The glucose tolerance tests during ketosis gave results similar to those found in adults by Linder, Hiller and Van Slyke; [3] Bang,[4] Staub,[5] Severinghaus [6] and others. The fasting blood sugar was lower than during the control period (chart 1, curve 2). The maximum rise occurred occasionally within one hour, but more frequently, later; this maximum was much higher than that in the control period, ranging from 180 to 346 mg. per hundred cubic centimeters of blood (chart 2, curve 4). The blood sugar content did not return to the fasting level within three hours. This delayed rise and fall of the curve is similar to that seen in a diabetic patient. We have called this type of blood sugar curve, occurring during ketosis, a diabetic blood sugar curve.

It was impossible in these cases to state when the diabetic blood sugar curve first appeared; as tests could not be performed daily, and all children do not have a ketosis on the first trial diet. In the cases in which tests were performed on the first day following the beginning of the ketogenic diet, a normal curve was obtained. There was not any correlation between the amount of acetone present in the urine and the height of the curve.

2. Woodyatt, R. T.: Objects and Method of Diet Adjustment in Diabetes, Arch. Int. Med. **28**:125 (Aug.) 1921.

3. Linder, G. C.; Hiller, H. A., and Van Slyke, D. D.: Carbohydrate Metabolism in Nephritis, J. Clin. Investigation **1**:247 (Feb.) 1925.

4. Bang, I.: Der Blutzucker, Münich, J. F. Bergmann, 1913.

5. Staub, H.: Untersuchungen über Zuckerstoffwechsel des Menchen, Ztschr. f. klin. Med. **93**:89, 1922.

6. Severinghaus, E. L.: The Effect of Fasting upon Carbohydrate Metabolism, J. Biol. Chem. **63**:48 (Feb.) 1925.

TABLE 1.—*Data Obtained in Cases of Ketosis Induced by Ketogenic Diet*

Case	Age	Sex	Diagnosis	Tolerance Test: Weight in Kg.	Tolerance Test: Sitting Height in Cm.	Tolerance Test: Gm. Glucose per Kg.	Date	Diet: Type	Diet: Days	Diet: Ketogenic	Diet: Antiketogenic	Diet: Total Calories	Acetone in Urine: Day of Appearance	Acetone in Urine: Amount	Acetone in Urine: Interval Between Disappearance and Test	Type Tolerance Curve	Blood Sugar Percentage: Fasting	½ Hour	1 Hour	1½ Hours	2 Hours	3 Hours
1	10	M	Chorea	25	68	1.5	12/10/25	Balanced	17		1:2.4	2,200	..	..	..	Normal	0.080	0.075	0.140	0.110	0.090	0.068
							12/14/25	Balanced	21		1:2.4	2,200	..	..	..	Normal	0.090	0.132	0.200	0.162	0.095	0.096
							12/17/25	Ketogenic	1	2.5:1		2,200	..	0	..	High normal	0.095	0.170	0.190	0.210	0.215	0.098
							12/21/25	Ketogenic	5	2.5:1		2,200	2	+++	..	Diabetic	0.095	0.170	0.215	0.270	0.346	0.176
							12/24/25	Balanced	3		1:2.4	2,200	..	0	1	Low	0.085	.....	0.105	0.120	0.105	0.115
							12/29/25	Balanced	8		1:2.4	2,200	..	0	6	Low normal	0.075	0.085	0.140	0.105	0.105	0.082
							1/ 2/26	Balanced	12		1:2.4	2,200	..	0	10	Low	0.085	0.115	0.105	0.125	0.150	0.070
							1/ 5/26	Balanced	15		1:2.4	2,200	..	0	13	Normal	0.082	0.134	0.204	0.138	0.112	0.098
2	8	F	Chorea	25	69	1.6	11/ 7/25	Balanced	41		1:2.4	1,666	..	..	..	Normal	0.100	0.140	0.140	0.156	0.092	0.105
							11/11/25	Ketogenic	3	2.5:1		1,661	3	+++	..	Diabetic	0.070	0.110	0.135	0.170	0.180	0.170
							11/13/25	Balanced	1		1:2.5	1,661	..	+	0	High normal	0.085	0.116	0.174	0.170	0.120	0.110
							11/16/25	Balanced	4		1:2.4	1,661	..	0	2	Low	0.080	0.100	0.086	0.093	0.083	0.080
							11/19/25	Balanced	7		1:2.4	1,661	..	0	5	Low	0.090	0.093	0.085	0.080	0.082	0.079
							11/24/25	Balanced	12		1:2.4	2,000	..	0	10	Low normal	0.090	0.118	0.132	0.130	0.118	0.100
							11/27/25	Balanced	15		1:2.4	2,000	..	0	13	Normal	0.118	0.144	0.168	0.140	0.120	0.120
							11/30/25	Balanced	18		1:2.4	2,000	..	0	16	Normal	0.092	0.092	0.141	0.142	0.120	0.100
							1/29/26	Balanced	78	.....	.....	.....	..	0	76	Normal	0.120	0.120	0.090	0.107	0.090	0.083
3	8	F	Chorea	31.4	76	1.3	11/ 6/25	Balanced	23		1:2.4	1,866	..	0	..	Normal	0.084	0.140	0.150	0.120	0.105	0.140
							11/11/25	Ketogenic	3	2.5:1		1,866	2	++	..	Diabetic	0.067	0.100	0.165	0.180	0.190	0.180
							11/13/25	Balanced	1		1:2.4	1,866	..	0	0	Low normal	0.110	0.135	0.115	0.115	0.110	0.100
							11/16/25	Balanced	4		1:2.4	1,866	..	0	3	Low	0.098	0.114	0.108	0.103	0.108	0.090
							11/19/25	Balanced	7		1:2.4	2,000	..	0	6	Low	0.095	0.125	0.101	0.085	0.085	0.085
							11/23/25	Balanced	11		1:2.4	2,000	..	0	10	Low	0.086	0.104	0.088	0.104	0.110	0.088
							11/27/25	Balanced	15		1:2.4	2,000	..	0	14	Normal	0.092	0.150	0.138	0.110	0.097	0.080
							11/30/25	Balanced	18		1:2.4	2,333	..	0	17	Normal	0.108	0.154	0.154	0.110	0.115	0.110
4	6	M	Chorea	22.7	61	1.4	2/ 5/25	Ketogenic	4	2.7:1		1,000	3	++	..	Diabetic	0.090	.....	0.140	.....	0.250	0.130
							2/21/25	Ketogenic	20	2.7:1		1,000	..	++	..	Diabetic	0.100	.....	0.280	.....	0.115	0.115
							2/25/25	Balanced	3		1:2.4	1,000	..	0	1	Low	0.090	.....	0.110	.....	0.110	0.105
				23	65	1.4	11/19/25	Balanced	35		1:2.4	1,666	..	..	..	Normal	0.083	0.140	0.100	0.100	0.097	0.074
							11/23/25	Balanced	39		1:2.4	1,666	..	..	..	Normal	0.110	0.162	0.158	0.136	0.143	0.096
							11/27/25	Ketogenic	4	2.5:1		1,666	2	+	..	Normal	0.075	0.140	.....	0.120	0.092	0.087
							11/30/25	Ketogenic	7	2.5:1		1,666	5	+	..	Normal	0.080	0.130	0.170	0.170	0.102	0.120
							12/ 3/25	Ketogenic	10	2.7:1		1,666	7	++	..	Diabetic	0.082	0.192	0.238	0.208	0.178	0.118
							12/ 7/25	Ketogenic	14	2.7:1		1,666	11	++	..	High normal	0.075	0.119	0.186	0.156	0.160	0.069
							12/10/25	Ketogenic	17	2.7:1		1,666	..	0	2	Low	0.095	0.118	0.130	0.110	0.115	0.104
							12/14/25	Balanced	4		1:2.4	1,666	..	0	6	Low	0.100	0.116	0.103	0.098	0.098	0.095
							12/17/25	Balanced	7		1:2.4	1,666	..	0	9	Normal	0.110	0.120	0.155	0.120	0.135	0.150
							12/21/25*	Balanced	11		1:2.4	1,666	2	++	..	Diabetic	0.090	0.095	0.112	0.122	0.225	0.076
							12/24/25†	Balanced	14		1:2.4	1,666	..	0	1	Low	0.080	0.105	0.080	0.105	0.110	0.082
							12/29/25	Balanced	19		1:2.4	1,666	..	0	6	Low	0.085	0.105	0.110	0.110	0.095	0.076

5	11	F	Chorea	27	70	1.5	4/ 6/25	Ketogenic	30	2.8:1	1,333	2	+	..	Diabetic	0.075	0.100	0.190	0.230	0.190	0.125
							4/10/25	Balanced	4	1:2.5	1,666	..	0	3	Normal	0.095	0.150	0.150	0.120	0.100	0.100
							4/13/25	Balanced	7	1:2.5	2,000	..	0	6	Low	0.075	0.116	0.108	0.100	0.090	0.080
							4/27/25	Balanced	21	1:2.5	2,000	..	0	20	Normal	0.095	0.110	0.176	0.140	0.100	0.078
							1/16/26	Balanced	240	?	?	..	0	?	Normal	0.105	0.110	0.140	0.115	0.087	0.095
6	12	F	Chorea	44.8	82	1.2	12/14/25	Balanced	21	1:2.4	2,333	..	0	..	Normal	0.090	0.133	0.175	0.125	0.098	0.088
							12/17/25	Ketogenic	1	2.5:1	2,333	0	0	..	Normal	0.092	0.150	0.138	0.110	0.097	0.097
							12/21/25	Ketogenic	5	2.5:1	2,333	4	++	..	Diabetic	0.110	0.090	0.220	0.220	0.235	0.150
							12/24/25	Balanced	2	1:2.4	2,333	..	0	0	High normal	0.070	0.120	0.150	0.160	0.160	0.110
							12/29/25	Balanced	7	1:2.4	2,333	..	0	5	High normal	0.069	0.085	0.130	0.130	0.100	0.100
							1/ 2/26	Balanced	11	1:2.4	2,333	..	0	9	Low	0.070	0.075	0.090	0.105	0.075	0.070
							1/ 6/26	Balanced	15	1:2.4	2,333	..	0	13	Normal	0.088	0.175	0.100	0.100	0.105	0.085
							1/ 7/26	Balanced	16	1:2.4	2,330	..	0	14	Low normal	0.094	0.120	0.130	0.090	0.102	0.065
9	7	M	Epilepsy (?)	26.5	61	1.5	10/22/25	Balanced	14	1:2.4	933	..	0	..	Normal	0.117	0.190	0.220	0.170	0.115	0.126
							11/ 4/25	Ketogenic	12	2.5:1	933	6	++	..	Diabetic	0.080	0.180	0.250	0.242	0.195	0.175
							11/ 6/25	Balanced	2	1:2.4	933	..	0	0	Normal	0.112	0.176	0.130	0.112	0.110	0.120
							11/ 9/25	Balanced	5	1:2.4	1,000	..	0	2	Low	0.110	0.120	0.128	0.108	0.108	0.112
							11/11/25	Balanced	7	1:2.4	1,000	..	0	4	Low normal	0.100	0.120	0.132	0.108	0.112	0.090
							11/13/25	Balanced	9	1:2.4	1,000	..	0	6	Low normal	0.110	0.135	0.126	0.110	0.098	0.084
							11/16/25	Balanced	12	1:2.4	1,000	..	0	9	Low	0.098	0.114	0.108	0.103	0.103	0.090
							1/10/26	Balanced	61	?	?	..	—	—	Normal	0.110	0.140	0.140	0.122	0.118	0.110
11	6	M	Chorea	23.6	69	1.7	6/ 7/26	Balanced	67	1:2.4	2,000	..	0	..	Normal	0.090	0.075	0.130	0.107	0.082	0.070
							6/12/26	Balanced	72	1:2.4	2,333	..	0	..	Normal	0.075	0.088	0.130	0.114	.....	.....
							6/14/26	Ketogenic	2	3:1	2,333	1	++	..	Diabetic	0.055	0.060	0.085	0.140	0.160	0.200
							6/19/26	Balanced	4	1:2.4	2,333	..	0	2	High normal	0.100	0.150	0.220	0.210	0.170	0.115
							6/21/26	Balanced	6	1:2.4	2,333	..	0	4	Normal	0.070	0.132	0.140	0.098	0.093	0.110
							6/23/25	Balanced	8	1:2.4	2,333	..	0	6	Normal	0.114	0.150	0.155	0.154	0.088	0.085
12	9	M	Chorea	36.3	77	1.3	6/ 8/26	Balanced	12	1:2.4	2,000	..	0	..	Low normal	0.082	0.100	0.104	0.120	0.094	0.086
							6/10/26	Balanced	14	1:2.4	2,000	..	0	..	Low normal	0.110	0.140	0.140	0.107	0.076	0.083
							6/14/26	Ketogenic	4	2.8:1	1,600	3	+	..	Diabetic	0.060	0.150	0.150	0.210	0.136	0.136
							6/17/26	Balanced	3	1:2.4	2,000	..	+	0	Normal	0.090	0.120	0.150	0.115	0.088	0.115
							6/23/26	Balanced	9	1:2.4	2,666	..	0	2	Normal	0.085	0.154	0.110	0.110	0.106	0.084
							6/28/26	Balanced	11	1:2.4	2,666	..	0	4	Low normal	0.068	0.120	0.107	0.092	0.068	0.068
13	10	F	Chorea	24.5	71	1.7	6/ 7/26	Balanced	10	1:2.4	1,333	..	0	..	Normal	0.079	0.107	0.140	0.110	0.120	0.087
							6/ 9/26	Balanced	12	1:2.4	1,333	..	0	..	Normal	0.105	0.150	0.122	0.120	0.110	0.065
							6/14/26	Ketogenic	4	2.7:1	1,333	2	0	..	Diabetic	0.050	0.085	0.175	0.220	0.180	0.146
							6/17/26	Balanced	2	1:2.4	2,000	..	0	0	High normal	0.077	0.128	0.220	0.190	0.087	0.058
							6/19/26	Balanced	4	1:2.4	2,000	..	0	2	High normal	0.115	0.210	0.240	0.180	0.140	0.075
							6/21/26	Balanced	6	1:2.4	2,000	..	0	4	High normal	0.081	0.150	.....	.....	0.083	0.075
							6/23/25	Balanced	8	1:2.4	2,000	..	0	6	High normal	0.135	0.138	0.220	0.142	0.124	0.080
							6/26/26	Balanced	11	1:2.4	2,000	..	0	9	Low	0.078	0.095	0.105	0.088	0.063	0.075
							6/28/26	Balanced	13	1:2.4	2,000	..	0	11	Low	0.075	0.097	0.118	0.105	0.100	0.078

* Fourth day of fever.
† First day of normal temperature.

The ketogenic diet was then changed to the regular diet which the patients had received on admission to the hospital. Their glucose tolerance was tested every three to five days thereafter until the curve returned to the normal.

After the children were back on the full diet, glucose tolerance tests showed in most cases that there was a transitional stage between the diabetic curve and the normal, which we have called the low blood sugar curve. During this transitional period, the fasting blood sugar was lower than in the normal control period and rarely lower than in the ketogenic period. The maximum was only from 10 to 35 mg. above

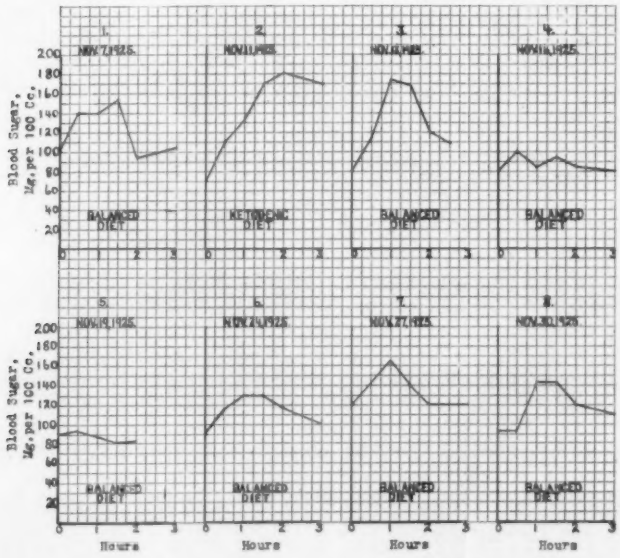

Chart 1 (case 2).—Glucose tolerance tests in a child with chorea; blood sugar curves obtained before, during and after ketosis induced by ketogenic diet; acetone in the urine was positive in only two instances (curves 2 and 3).

the fasting blood sugar (chart 1, curves 4 and 5), and the blood sugar returned to the fasting level within two hours and often within one hour (chart 3, curve 7). The curve was characterized by a rapid rise and fall, the total rise being usually of small amplitude.

This low blood sugar curve appeared usually from three to four days after the discontinuance of the ketogenic diet. In case 5, it did not appear until the sixth day, and in case 6, it appeared on the ninth day (chart 3, curve 6). If a glucose tolerance test was performed before this time, a normal or high normal curve was obtained (chart 1, curve 3). This low blood sugar curve generally persisted for about eight days, after which the normal tolerance for glucose was obtained.

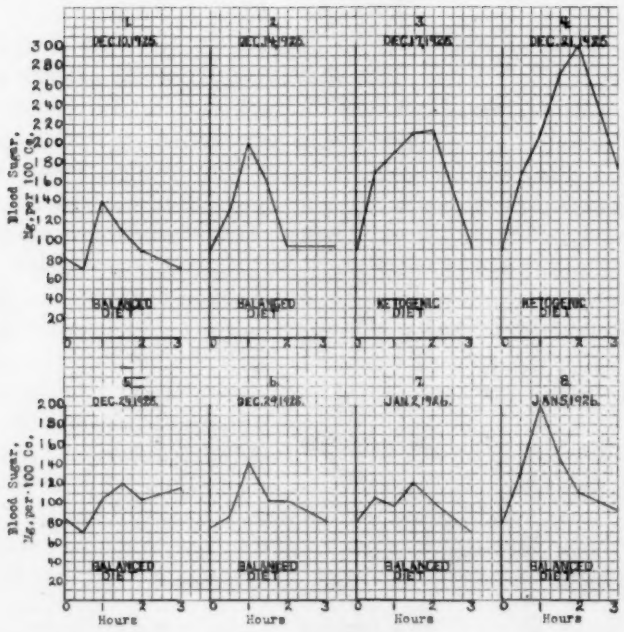

Chart 2 (case 1).—Glucose tolerance tests in a child with chorea; blood sugar curves obtained before, during and after ketosis induced by ketogenic diet; acetone in the urine was positive in only one instance (curve 4).

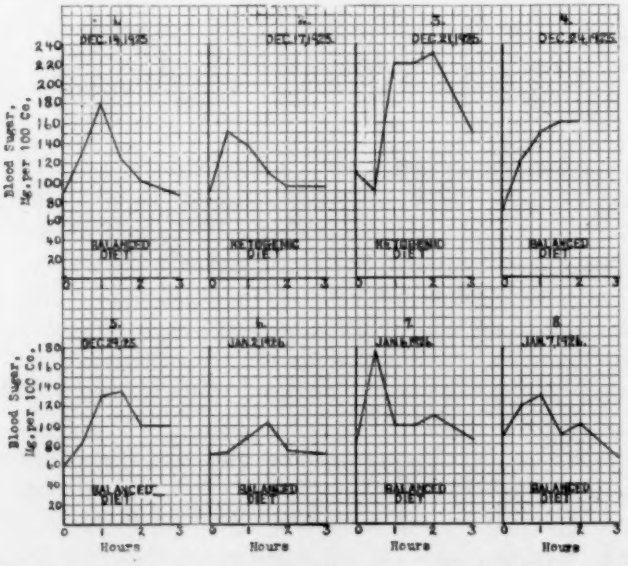

Chart 3 (case 6).—Glucose tolerance tests in a child with chorea; blood sugar curves obtained before, during and after ketosis induced by ketogenic diet; acetone in the urine was positive in only one instance (curve 2).

TABLE 2.—*Data Obtained in Cases of Ketosis Following Cyclic Vomiting*

Case	Age	Sex	Weight in Kg.	Sitting Height in Cm.	Tolerance Test: Gm. Glucose per Kg.	Tolerance Test: Date	Diet: Number Days Vomiting	Diet: After Vomiting	Diet: Days	Diet: Total Calories	Acetone in Urine: Days	Acetone in Urine: Days Free	Type Tolerance Curve	Blood Sugar Percentage: Fasting	½ Hour	1 Hour	1½ Hours	2 Hours	3 Hours
7	4	M	13.6	50	...	.....	4	High carbohydrate	..	.....	4								
					2.2	1/ 9/25	..	Balanced	2	733	..	2	Low normal	0.087	0.090	0.110	0.095	0.075	0.095
						1/11/25	..	Balanced	4	1,000	..	4	High normal	0.110	0.118	0.150	0.163	0.165	0.075
						1/15/25	..	Balanced	8	1,333	..	8	Low	0.095	0.110	0.100	0.105	0.095	0.093
						1/19/25	..	Balanced	12	1,333	..	12	Low	0.120	0.134	0.118	0.115	0.115	0.110
8	4	F	15.0	55	...	.....	7	High carbohydrate	..	.....	6								
					2.7	3/ 4/25	..	Balanced	2	666	..	4	Normal	0.085	0.085	0.080	0.150	0.130	0.100
						3/ 6/25	..	Balanced	4	666	..	6	Normal	0.085	0.110	0.100	0.125	0.134	0.100
						3/10/25	..	Balanced	8	666	..	10	Low	0.072	0.110	0.108	0.110	0.100	0.085
						1/16/26	..	Balanced	307	?	..	..	Normal	0.090	0.120	0.150	0.122	0.102	0.090
10	5	F	15.0	58	...	.....	5	.....	..	.....	8								
					1.8	12/ 6/24	..	Balanced	4	1,100	..	4	Normal	0.105	0.135	0.140	0.140	0.140	0.100
					2.6	12/ 8/24	..	Balanced	6	1,100	..	6	Normal	0.100	0.120	.....	0.200	0.120	0.110
					1.8	12/17/24	..	Balanced	15	1,100	..	15	Normal	0.100	0.140	0.140	0.120	0.130	0.100

The acetone in the urine disappeared between the first and third days, following the restoration of the regular diet.

The second group consisted of three children admitted to the hospital in a state of ketosis due to cyclic vomiting. All the children were severely ill, being in a comatose or semicomatose state. On admission, glucose was given intravenously, and saline by subcutaneous injection. Glucose was also given by rectum. Until these children were able to take nourishment by mouth, this para-enteral administration of fluids was continued. Determinations for blood sugar made one hour after administration of glucose, while the children were still vomiting, were always high. For example, patient 7 had a blood sugar of 0.440 mg. per hundred cubic centimeters. As soon as food was retained, a diet rich in carbohydrates was administered.

A glucose tolerance test was performed as soon as practicable: in case 8, five days after admission; in case 7, four days after admission, and in case 10, six days after admission. The blood sugar curves, at first, were of either a high normal or a normal type (chart 4, curves 1 and 2). Then, in a few days, two patients developed a low blood sugar curve

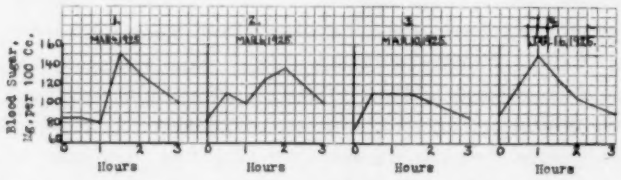

Chart 4 (case 8).—Glucose tolerance tests in a child with cyclic vomiting; blood sugar curves obtained after ketosis induced by an attack of cyclic vomiting; in each instance (curves 1 to 4) the diet was balanced, and acetone in the urine was negative.

(chart 4, curve 3), similar to that observed in the first group of cases following the induced ketosis. This low blood sugar curve lasted until the patients were discharged from the hospital. Patient 8 returned to the clinic nine months later and had a normal blood sugar curve (chart 4, curve 4); patient 7 returned two months later in another attack of cyclic vomiting, and died twenty-four hours after admission. A postmortem examination did not show anything specific. All the organs showed evidence of cloudy swelling often seen in an acute toxic condition.

At present, sugar tolerance tests are being made on children after an acute febrile infection, such as lobar pneumonia or a nasopharyngitis. Acetone is usually present in the urine during the febrile period. Tolerance tests made after the cessation of fever often give results different from those after an induced ketosis. These reactions will be discussed in another paper.

COMMENT

Many have attempted to explain the cause of low fasting blood sugar and a reduced glucose tolerance during ketosis. The low fasting sugar may be due to the fact that during starvation or during a low carbohydrate and high fat diet, a diminution of the glycogen stores occurs rapidly. Less carbohydrate is, therefore, available for output into the blood, and perhaps the body conserves its already diminished glycogen stores. Nagasuye,[7] Bang,[4] Cori and Cori,[8] and others have found that the glycogen content of animal tissue is low after a long fast or after a few days on a ketogenic diet. Markowitz[9] has shown that long starvation does not render the liver entirely glycogen-free.

The attempted explanation of the diabetic type of sugar curve during ketosis is that following a low carbohydrate diet the organism is unable to adjust itself rapidly to metabolize a large amount of carbohydrate. It is difficult to state whether this reaction is due to an inability to mobilize insulin or the inability of the liver to form glycogen. Bang concluded that the liver of a fasting animal was not able to form glycogen. Barrenscheen[10] found that the liver of a starved animal, when perfused with glucose solution, did not take up glucose or make glycogen as did the liver of a normally fed animal. Goldblatt[11] believes that there is some deficiency in the storage and oxidation of glycogen after starvation. Severinghaus[6] believes that this inability to store glycogen is due either to an inhibition of insulin formation, or to the fact that insulin cannot function during an acidosis. However, Kageura,[12] Linder, Hiller and Van Slyke,[3] and others state that the acidosis is not the cause of the abnormal blood sugar curves.

Following the introduction of the ketogenic diet, the time of appearance of the diabetic blood sugar curve varies, as already mentioned, with each child. It depends, probably, on the child's previous carbohydrate storage and also on the individual ability to store fat given in the diet. As Levine, Rivkin and Wilson[13] have shown, the ketogenic-

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7. Nagasuye, Shi: Experimentelle Untersuchungen über die Assimilation der Lavulose, Galaktose und der Glykose bei Hunger und Eiweissfett-diät, J. Biochem. **5**:449 (Oct.) 1925.

8. Cori, C. F., and Cori, G. T.: The Fate of Sugar in the Animal Body, J. Biol. Chem. **70**:557 (Oct.) 1926.

9. Markowitz, J.: Glyconeogenesis, Am. J. Physiol. **74**:22 (Sept.) 1925.

10. Barrenscheen, H. K.: Ueber Glykogen und Zuckerbildung in der isolierten Warmblut Leber, Biochem. Ztschr. **58**:277, 1913.

11. Goldblatt, M. W.: Observations on the Effect of Various Carbohydrates on the Ketosis of Starvation in Human Subjects, Biochem. J. **19**:948, 1925.

12. Kageura, N.: Ueber den Einfluss der Eiweiss-Fettdiät auf den Kohlenhydratstoffweschsel, J. Biochem. **2**:341 (Jan.) 1923.

13. Levine, S. Z.; Rivkin, H., and Wilson, J. R.: Respiratory Metabolism in Infancy and Childhood Glycogen Storage in Children, Am. J. Dis. Child. **31**:496 (April) 1926.

antiketogenic ratio necessary to produce a ketosis is higher in some children than in others, because some children store fat more easily. They also have shown that the sugar metabolism of children subject to cyclic vomiting is normal between attacks.

Following the period of ketosis, when the carbohydrate storage of the organism was depleted, an adequate, well balanced diet was again administered. From three to four days was required before a child would regain his ability to utilize carbohydrate properly. This was evidenced by the gradual change of the diabetic type of blood sugar curve. Kageura,[14] in a few instances, obtained low blood sugar curves when giving glucose tests after ketogenic diet. This low blood sugar curve can be explained, perhaps, by the fact that following the restoration of normal carbohydrate function, the tissue cells may have an increased avidity for carbohydrate in order to replenish their depleted storage. Bernstein and Falta [15] state that after starvation, glucose is first stored as glycogen, and that ingested carbohydrate is burned only when the glycogen depots are filled.

Another explanation of this low blood sugar curve is offered by Thalhimer.[16] He suggests that there may be an oversecretion or increased output of insulin following ketosis, because of overcompensation on the part of the body or the mechanism which secretes insulin. This oversecretion or increased output would seem to be a continuation of the reaction which occurs in response to the need for more insulin during ketosis. An interesting reference in favor of Thalhimer's view is that of Eisner.[17] Eisner obtained a low curve in rabbits which received, in addition to their regular food, an excessive amount of glucose. For the first few days, the blood sugar curves were normal, and later the low blood sugar curve was obtained. At this time, when the low blood sugar curve was obtained, the glycogen content of the tissues of the animals was high. An oversecretion of insulin takes place, perhaps, in order to take care of the excessive carbohydrate. Eisner believes, however, that when the tissues are filled with glycogen, there is little need to burn glucose and that the liver is not stimulated to give out glycogen.

Unfortunately, we did not determine the inorganic phosphates of the blood during the tolerance tests. Hartman and Bolliger [18] have

14. Kageura, N.: Ueber den Einfluss der Eiweiss-Fettdiät auf den Kohlenhydratstoffweschsel, J. Biochem. **1**:333 (July) 1922.

15. Bernstein, S., and Falta, W.: Respiratorischer Stoffwechsel und Blutzuckerregulation, Deutsches Arch. f. klin. Med. **125**:233, 1918.

16. Thalhimer, W.: Personal communication to the author.

17. Eisner, G.: Ernährungschadingungen in ihrer Bedeutung für Blutzucker und Glykogengehalt der Organe (Studium zum Kohlenhydratsoffwechsel), Ztschr. f. d. ges. exper. Med. **52**:214 (Sept.) 1926.

18. Hartman, F. W., and Bolliger, A.: Curve of Inorganic Blood Phosphates During the Sugar Tolerance Test, J. A. M. A. **85**:653 (Aug. 29) 1925.

shown that normally, during a glucose tolerance test, the inorganic phosphorus is lowered and that it rises to the normal level at the end of three hours. In a diabetic patient, however, the inorganic phosphorus remains low at the conclusion of the test. These authors state that the presence of insulin is as essential for the utilization of phosphates as it is for the utilization of carbohydrate.

SUMMARY

I. Glucose tolerance tests were made on nine children before, during and after a ketosis, induced by a ketogenic diet.

A. Before the ketosis, normal blood sugar curves were obtained.

B. During the ketosis:

1. The fasting blood sugar was lower than the normal blood sugar.

2. The maximum rise of the blood sugar was much higher than the normal and usually delayed. The blood sugar did not return to the fasting level within three hours, and, therefore, this curve resembled the diabetic blood sugar curve.

C. After the ketogenic diet was discontinued:

1. The fasting blood sugar was lower than normal but not as low as during ketosis.

2. A normal or high blood sugar curve was obtained for the first three to five days in seven of the cases, for six days in one case and for eight days in another.

3. A low blood sugar curve was then obtained which persisted for about eight days. This was characterized by a small maximum rise (about 10 to 35 mg.) and a rapid return to the fasting blood sugar level, frequently within one hour and always within two hours.

II. Glucose tolerance tests were made on three children following ketosis caused by cyclic vomiting.

A. A normal or high blood sugar curve was obtained for the first six days after the cessation of vomiting.

B. A low blood sugar curve was obtained in two of the cases after the sixth day. The duration of this low blood sugar curve could not be determined. One of the children who had a low blood sugar curve on discharge from the hospital had a normal curve when tested one year later.

CONCLUSIONS

1. During ketosis induced by a ketogenic diet, there is a disturbance of carbohydrate metabolism, as evidenced by the delayed reaction of the blood sugar following a glucose tolerance test.

2. After the cessation of a ketosis induced by a ketogenic diet, the carbohydrate metabolism does not return to normal at once, but passes through a transitory stage during which there appears to be an excessive ability to utilize carbohydrate, as shown by the occurrence of only a slight rise in the blood sugar curve following a glucose tolerance test.

3. Following recovery from ketosis caused by cyclic vomiting, there is also a transitory stage, as evidenced by the low normal blood sugar tolerance curve.

4. This low normal blood sugar tolerance curve, following ketosis, may be due to an oversecretion or an increased output of insulin.

FEEDING CARE OF THE INFANT IN THE OBSTETRIC NURSERY*

FRANK C. NEFF, M.D.
KANSAS CITY, MO.

With the increasing percentage of births occurring in the hospital, it is pertinent to inquire how well the nursing and nutrition of the infant during the new-born period can be managed in an institution. From the tenth to the fourteenth day, when the hospital stay is usually completed, the infant should have made satisfactory gains, and it is desirable to have it reach or exceed the initial weight. Much can be done to increase the percentage of successful feeding and proper nutrition during this period.

The material for this paper was gathered from the experiences in the nursery of the General Hospital in Kansas City during my service or that of my colleagues. It has been made possible chiefly through the practice of measuring and recording all breast feedings for the past three years. During this time I have been especially interested in the incidence of the recovery of the birth weight.

The first table shows an analysis of the records of 678 infants, classified according to the weight at birth, and separated into two groups determined by the progress attained at the age of 12 days. The number of infants weighing under 5 and over 9 pounds (2.3 and 4.1 Kg.) is too small to be of value for conclusions, but these were necessarily included in obtaining the totals. What few sick infants there were have been excluded.

The analysis of these comparisons between 342 infants not regaining their birth weight and 336 infants who did so by the twelfth day shows the relative average physiologic loss, the average day of maximum loss and the percentage of those at each birth weight level attaining the more desirable increase. The average day of early regaining weight is also recorded.

AVERAGE DAY OF MAXIMUM PHYSIOLOGIC LOSS OF WEIGHT

In both groups it will be noticed that the infants whose weight averaged 3 pounds (1.4 Kg.) lost weight somewhat earlier than at the other levels. Both groups in which weight at birth was 4 pounds (1.8 Kg.) were the latest in losing. The number of these premature infants is too small for drawing conclusions.

* Received for publication, June 1, 1927.
* Read before the meeting of the American Pediatric Society, May 13, 1927.

A definite difference is found in the day of maximum loss between the two general groups. All of those infants who regained their birth weight had an average physiologic loss earlier than those in group 1.

AMOUNT OF PHYSIOLOGIC LOSS

In nearly all instances the average loss increased with the amount of the initial weight. In the second group this increase is regular in the infants weighing up to 10 pounds (4.5 Kg).

The figures for the two groups show that infants who regained their weight have a definitely smaller loss during the early inanition period than have those who failed to regain by the time they were 12 days of age. This is of especial interest in the large number of infants at the weight of 7 pounds (3.2 Kg.). Here the amount in group 2 is

TABLE 1.—*Average Weight Changes in 678 Consecutive New-Born Infants; Ratio of Weight at Birth to That at the Age of 12 Days*

Birth Weight		Group 1 Below at 12 Days of Age				Group 2 Above at 12 Days of Age					Percentage of 678 Infants at or Above Birth Weight on Twelfth Day
		Total Number of Infants	Day of Maximum Loss	Average Physiologic Loss		Average Physiologic Loss		Day of Maximum Loss	Total Number of Infants	Day of Regaining Birth Weight	
Lb.	Gm.			Oz.	Gm.	Oz.	Gm.				
3	1,360	4	2.75	6.5	184	1.5	42	1.00	2	7.00	33.3
4	1,814	2	4.5	8.25	233	3.81	108	3.27	11	8.72	84.6
5	2,267	32	3.68	7.09	201	5.07	143	2.20	26	7.11	44.8
6	2,727	56	2.82	7.0	198	5.27	149	2.38	91	7.25	61.9
7	3,175	140	3.07	9.09	253	5.52	156	2.17	147	7.26	51.2
8	3,628	70	3.16	8.71	246	7.0	198	2.43	42	7.24	37.5
9	4,082	32	2.78	10.34	293	8.20	232	2.20	15	8.04	31.9
10	4,535	6	3.66	12.50	354	7.0	198	2.50	2	7.5	25.0
Total.....		342	....	....	....	....	....	....	336		
Average.....		...	3.30	8.68	246	5.42	153	2.26	...	7.51	46.2

5.52 ounces (0.14 Kg.) as compared with 9.09 (0.3 Kg.) ounces in group 1. At the weight levels of 4 and 10 pounds (1.8 and 4.5 Kg.), the difference is the greatest, their ratio being, respectively, from 3.81 to 8.25 ounces (0.09 to 0.21 Kg.) in 4 pound infants and from 7 to 12.5 ounces (0.18 to 0.31 Kg.) in 10 pound infants.

INFANTS REGAINING BIRTH WEIGHT—AVERAGE DAY AND PERCENTAGE

The average time of regaining birth weight in the second group is seven and one-half days.

In 678 infants, 46.2 per cent regained their weight during the twelve day period. The average percentage for 7 and 6 pound (3.2 and 2.7 Kg.) babies is higher than any except for those at 4 pounds (1.8 Kg.). The percentages for these weights are respectively 51.2, 61.9 and 84.6. The explanation of the large proportion of 4 pound babies who regained their weight, in an average of 8.7 days, lies in the custom of forcing the feeding of these premature infants with expressed breast milk.

BREAST-NURSING

Some mothers coming to full term have demonstrable evidences of colostrum before the baby is born. During labor it is not uncommon for milk to escape from the nipples. In 42 per cent of the cases in this series as much as from 1 to 6 ounces (0.025 to 0.15 Kg.) were obtained from the mother's breasts in the first twenty-four hours. On the contrary, two mothers had dry breasts up to the tenth day, but after convalescence and leaving the bed, the milk came in sufficiently for the complete nursing of their babies.

Table 2 is made up of records from six selected cases, showing the presence of from 2.5 to 4 ounces (0.06 to 0.1 Kg.) of breast milk

TABLE 2.—*Infants Getting Milk from Breast on First and Second Days*

Day of life	1	2	3	4	5	6	7	8	9	10	11	12
No. 38												
Breast milk....oz.	..	5	8	15	18	16	19	19	21	21	18	19
Formula....oz.	1	2.5	2.25	..	..	..	..	..	..	..	..	..
Weight....lbs.-oz.	6-13	6-10	6-7	6-7	6-10	6-11	6-11	6-15	7	7-1	7-3	7-6
No. 60												
Breast milk....oz.	4	4	8.25	14	13	14	14	18	18	17		
Formula....oz.	3.25	3	2	..	..	..	..	..	..	..	..	..
Weight....lbs.-oz.	8-3	7-13	7-9	7-10	7-14	8-2	8-4	8-4	8-4	8-4	8-4	8-6
No. 64												
Breast milk....oz.	3.5	7.5	14.75	23	18	20	24	22	22	18	18	
Formula....oz.	..	..	..	..	..	..	..	..	..	..	..	..
Weight....lbs.-oz.	7-8	7-4	7-5	7-6	7-10	7-11	7-13	7-14	7-15	8	8	8-2
No. 75												
Breast milk....oz.	3.5	11	12	17	20	16	18	19	24	19	23	21
Formula....oz.	..	..	..	..	..	..	..	..	..	..	..	..
Weight....lbs.-oz.	8-8	8-5	8-6	8-7	8-9	8-10	8-10	8-12	8-13	8-12	8-12	8-14
No. 87												
Breast milk....oz.	2.5	2.5	5	10	15	18	14	14	14	19	13	14
Formula....oz.	..	1.5	2.75	1	..	..	..	..	..	..	..	..
Weight....lbs.-oz.	7-8	7-5	7-5	7-4	7-6	7-6	7-8	7-8	7-9	7-13	7-12	7-14
No. 88												
Breast milk....oz.	..	3.75	3	10	13.5	18	17	17	17	17	17	
Formula....oz.	1.75	1.75	1.25	1.5	..	..	..	..	..	..	..	
Weight....lbs.-oz.	6-13	6-12	6-10	6-10	6-12	6-14	6-15	6-15	7-2	7-2	7-2	

nursed by four infants on the first day. Numbers 38 and 88 got their first breast milk on the second day, and on the tenth day one of these took more milk than any of the others. All of these exceeded their birth weight by the ninth day.

The nursing routine is to put the child to the breast every eight hours in the first twenty-four, and every four hours, day and night, thereafter. The infants get complemental and three supplemental feedings on the first day. Until the milk becomes sufficient for sustained attempts at nursing the infant remains at the breast only three minutes, and thereafter only from five to eight minutes. It was apparent that the incidence of cracked nipples was reduced by these short periods. Each nursing until the yield is established, or if the breasts are uncomfortably full, is followed by manual expression. This practice apparently increases the supply for the infant, makes the mother's condition more tolerable and furnishes enough for the feeding of our premature infants.

Table 3 is an analysis of a particularly favorable group of infants, representing ninety-one consecutive births during the months of March and April, 1927. Forty of these infants are not included in table 1. The percentage of infants above weight at 12 days was 69.3,

TABLE 3.—*Amount of Milk Taken During the New-Born Period by Ninety-One Consecutive Infants* *

Day	Group 1 Average of Sixty-Three Infants Above Weight on Twelfth Day		Group 2 Average of Twenty-Eight Infants Below Initial Weight		Group 1 Average Amount Taken at a Feeding,	Physiologic Capacity of Stomach (Scammon and Doyle)
	Oz.	Cc.	Oz.	Cc.	Cc.	Cc.
1	2.6	78	2.1	63	13	9
2	6.4	192	6.5	195	32	22
3	9.8	294	7.3	219	49	43
4	13.2	396	10.8	324	66	65
5	15	450	13.1	393	75	78
6	15.5	465	13	390	77	85
7	16.5	495	13	390	82	90
8	16.5	498	14.3	429	83	94
9	16.6	498	15.2	456	83	99
10	17	510	17	510	85	105
11	17.2	514	21	630	..	..
12	17.3	519	16.5	495	..	..

* In gaining infants the amount of breast milk taken during the twelve day period averaged 4,939 cc., and in nongaining infants 4,494 cc., with a definitely smaller intake from the third to the ninth day, inclusive. After the ninth day, both groups got about the same amount.

TABLE 4.—*Mixed Feeding During Physiologic Inanition Period*

Day of life	1	2	3	4	5	6	7	8	9	10	11	12
No. 1												
Breast milk....oz.	..	1	2	4	10	..	..	3	8.5	3	3	..
Formula....oz.	1.25	3.25	5	7.5	5	14	18.5	14.5	11.5	18	18	20
Weight....lbs.-oz.	5-10	5-8	5-7	5-7	5-8	5-10	5-11	5-13	5-14	5-11	5-12	5-14
No. 16												
Breast milk....oz.	..	1	4	4	9	11	12	14	23	17	19	23
Formula....oz.	1.75	3.75	5.5	7	6.75	5	2	..	..	..	..	..
Weight....lbs.-oz.	9-5	9	8-11	8-10	8-13	8-12	8-11	8-12	8-10	8-13	8-11	8-10
No. 53												
Breast milk....oz.	..	..	..	..	..	10	11	13	14	16	19	15
Formula....oz.	1.5	7.5	7.75	9	12	2.5	..	..	..	..	..	..
Weight....lbs.-oz.	7-4	7-2	7-1	7	7-1	7-3	7-6	7-5	7-5	7-6	7-8	7-9
No. 78												
Breast milk....oz.	..	..	10	12	15	16	15	20	17	16	19	16
Formula....oz.	2.25	4.25	1.75	1	..	..	..	..	..	..	..	..
Weight....lbs.-oz.	8-4	7-14	7-14	7-15	7-15	8	8	8	8-3	8-3	8-4	8-4
No. 81												
Breast milk....oz.	..	..	3	5.75	6	10	12	13	15	14	15	11
Formula....oz.	1.5	3.75	4.25	1.25	2.75	1	..	..	..	..	..	..
Weight....lbs.-oz.	6-7	6-5	6-4	6-1	6-5	6-4	6-5	6-5	6-6	6-7	6-8	6-10
No. 82												
Breast milk....oz.	..	3	8	13	14	15	14	13	17			
Formula....oz.	4	5	1.25	..	..	..	..	..	..	..		
Weight....lbs.-oz.	8-8	8-4	8-5	8-6	8-6	8-6	8-7	8-6	8-9	8-10		

all of whom received more milk during the first nine days than did the less fortunate group. Otherwise, the amounts received daily are not of especial interest. The average feeding received is noted on each day, and in the last column is placed, for comparison, the figures given by Scammon and Doyle for the physiologic capacity of the stomach. In my figures, the intake per feeding is greater for the first four days and less for the next six days than those of Scammon and Doyle.

As an illustration of the excessive amount which may be taken by breast-fed babies in unregulated nursing, I found one infant in another nursery getting on the seventh day an average of 5 ounces (1.3 Kg.) at the breast every three hours, day and night, making 40 ounces (1.1 Kg.) in all. This overfeeding had caused vomiting and diarrhea.

In table 4 are recorded the daily intake and weight of six infants who did not receive any breast milk on the first day and who received little on the second day. One did not take any until the sixth day, when a plentiful supply developed. In such instances the nursery has used complemental feeding, beginning after each breast feeding on the first day and continuing thereafter as shown in table 4. Infant 1 was fed a formula preparation throughout the new-born period, because of

TABLE 5.—*Comparison of Amounts Taken in Twenty-Four Hours at Complete Breast and Mixed Feeding*

Day	1	2	3	4	5	6	7	8	9	10
Average for 24 hours of complete breast feeding, oz.	1.3	6.7	10.1	13.3	15	15.7	16.2	17.2	17	17.8
Mixed feeding during physiologic inanition period only..... oz.	2.3	4.7	7.7	12.5	14.8	15.6	16.2	17.1	17	17.2

TABLE 6.—*Average Quantities in Entirely Breast-Fed Full Term Infants Failing to Gain*

	1	2	3	4	5	6	7	8	9	10
Average of ounces in 24 hours.....	0.5	3	3	5.5	6	8	6.5	9.7	9	10

tuberculosis in the mother. The other five received complemental feedings during from three to seven days. These are selected cases, showing successful gains in weight and the indication for discontinuing mixed feeding as soon as the breast milk is sufficient.

Table 5 shows that the yield from the breasts is about the same after the fifth day for infants given breast milk alone, or mixed feeding at the start. Therefore, a close parallelism has been found in the nursery in the amount taken on the second five days, whether or not the child has mixed feeding for the first few days.

The chief advantage in using mixed feeding from the beginning is found in those infants who receive a minimum of breast milk throughout the entire new-born period. The average quantities in entirely breast-fed, full term infants (table 6) were not accompanied by any gain in weight.

It is possible that many of this group nursed more from the breasts after the mother recuperated from her lying-in period.

COMMENT

Eighty-two per cent of all the babies that left the hospital were entirely breast fed; 16 per cent received mixed feeding and 2 per cent bottle feeding alone. In the recent series of ninety-one infants, all but one child were entirely breast fed when they left the hospital; this probably was due to the increased efforts and accumulated experience in nursing technic.

The nursery from which figures have been collected belongs to a general charity hospital. It is conceded that the class of patients from this social level is more apt to have an adequate supply of breast milk. Other factors which influence a high percentage of breast feeding are probably present to a greater degree than in private hospitals. Good prenatal care is given as regards syphilis, nephritis and retracted nipples. The control of the patients is good. The nursing technic has been under the active administration of the same supervising nurse for the past three years. Although the quarters are small, every effort is made to prevent infections and to increase the yield of breast milk. Pemphigus is the only extensive epidemic that has occurred.

It is obvious that some physiologic loss of weight is unavoidable, and probably beneficial, as regards the stimulation of nursing by hunger. It is advisable to recognize the time when inanition weight loss has passed the physiologic period and to use all efforts to increase the secretion of breast milk. Especially in the primipara, but sometimes in the multipara, successful breast nursing cannot be predicted in the individual case, though it should be expected.

The routine of complemental feeding for the first few days of life has been conducted as an experiment for the past three years; in this nursery it seems that, combined with energetic efforts to send the infant home entirely on breast feeding, the welfare in many cases has been increased by the mixed feeding. For this purpose a mixture of 10 parts of boiled whole milk, with or without acidulation, 1 part of syrup and 5 parts of water is now being used; the food value of this preparation is 20 calories per ounce.

CONCLUSIONS

1. In the hospital nursery the early feeding needs are well determined if the technic of nursing and the care of the infant are carefully supervised.

2. Records of 718 new-born infants are tabulated and discussed from the standpoints of feeding and weight.

3. In the first series of 678 infants, from 25 to 84.6 per cent, depending on the weight at birth, had regained or exceeded this weight at the twelfth day. In the second series of ninety-one consecutive

infants, fifty of whom were included in the first series, 69.3 per cent regained their birth weight.

4. Infants who have their maximum physiologic loss earliest are the first to regain their weight. Likewise those who lose the least, regain the quickest. Regaining is dependent on many other factors, and, all else being favorable, chiefly on adequate amounts of food throughout the twelve day period.

5. Sufficient milk to be of some help in the first twenty-four hours is present in 42 per cent of mothers; in most of the mothers in the cases reported here, it was present on the second day. Regular nursing and manual expression on and after the first day have apparently increased the yield and have made complete nursing possible when, in some cases, it would not otherwise have resulted.

6. Carefully controlled complemental feeding is helpful when milk is scanty or absent in the early days. When discontinued at the proper time adverse influence on later lactation has not been evident.

7. Eighty-two per cent of all infants that left the hospital were entirely breast fed, and 2 per cent were bottle fed. Sixteen per cent of the mothers seemed incapable of supplying enough milk for optimal gains in their infants, at least during the twelve days in the hospital; in these cases complemental feedings were used.

Progress in Pediatrics

THE TECHNIC OF TEACHING*

JOHN LOVETT MORSE, A.M., M.D.
Professor of Pediatrics, Emeritus, Medical School of Harvard University
BOSTON

My topic should really be "The Technic of Teaching Medicine," as this is the only kind of teaching about which I know anything. It should be still further limited, perhaps, to "The Technic of Teaching Pediatrics," as this is the kind of medical teaching that I have chiefly done. The teacher of medicine has an advantage over most teachers in that his students are not only willing but anxious to be taught. It is hard enough to teach even students of this sort. I cannot think of anything more difficult than to teach students who are not interested or who do not wish to learn.

To teach well, a man must like to teach. He must be interested in his teaching and must be willing to sacrifice everything else to it. If a conflict arises between his teaching and his private practice or consultations, he must be willing to let his practice and consultations go in order to teach. He must never cut an exercise, unless he or some one in his family is ill. He must not call on others to take his place at short notice, because no one can take his place without due preparation. Furthermore, he must be willing to put all he has into his teaching. It is impossible to "put it over" otherwise. He must not spare himself. He can be sure that if he is not thoroughly tired out after an exercise, his exercise has not been successful.

A teacher must know his subject thoroughly. More than this, he must have his knowledge clearly and definitely arranged in his mind. He must know just what he thinks about everything. Furthermore, he must appreciate what he does not know and must be able to tell his students that he does not know in such a way that they do not lose confidence in him. He must be able to tell what he knows clearly. He cannot do this unless he thinks clearly. A man who does not think clearly and who cannot tell others clearly what he thinks should not attempt to teach. Unfortunately, there are many who do not think clearly and many more who think clearly but who cannot express themselves clearly.

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* Address delivered before the Association of American Teachers of Diseases of Children, Washington, D. C., May 17, 1927.

A teacher must appreciate and keep in mind what his students are expected to know about his subject. He must understand what the men in a given class should know and he must fit his teaching to their knowledge. An entirely different type of teaching is necessary for men in different years of the course. In the early years, the students know a great deal about laboratory medicine, physiology, chemistry, etc.; in fact, they probably know more than their instructor, if he is a clinician. On the other hand, they know little in a practical way about disease and its manifestations in patients. In these years, the teaching in clinical subjects must be along broad lines, and general principles should be emphasized. In the later years, the teaching should go more into detail and finer points should be considered. It is important never to talk over the heads of the students. A teacher should never take up much time talking about minor points and should never more than mention investigations in which he himself is especially interested. When there is a difference of opinion among authorities about certain points, he should give the generally accepted view and merely refer to the others. If he does not, he is certain to confuse young students. It is also important for him to emphasize rules rather than exceptions, because the student always remembers the exception and forgets the rule.

Graduate students must be taught in a different way from undergraduates. They are of different types, and each type must be taught in a different way. The teacher must appreciate their point of view and try to give them what they want to know. Physicians who come, as they say, to "brush up" or to take a short course in a specialty are usually short on laboratory knowledge and long on experience. They want, and should be given, practical points to help them in their practice. They need, and should be given, summaries of new knowledge and methods. Physicians who are training to be specialists and who are putting in months or years in acquiring this training need opportunities and supervision more than teaching. They should be given these.

There are many different types of teaching. I shall take them up separately, as they deserve individual consideration.

THE DIDACTIC LECTURE

I thoroughly believe that there is still a place for the didactic lecture in the teaching of medicine and of the diseases of children. In my opinion, there is nothing else that can take its place. There is no other way in which the student can be given such a clear and definite picture of disease. He cannot get it from reading, because he is not competent to determine what is important and what is unimportant. He cannot get it from experience except after many years of practice. The didactic lecture must be given, however, by a man of wide experience, who has a clear picture of disease acquired from his own experience. He must

be able to bring out the salient points, and to sift the chaff from the wheat and the important from the unimportant. He must be able to paint a picture that the student will never forget. Such a lecture requires hours of preparation, thought and study on a background of vast clinical experience. It cannot be given by glancing over, just before going to the exercise, notes made five, ten or twenty years previously.

THE AMPHITHEATER CLINIC FOR LARGE CLASSES

To my mind, there is still a place for the amphitheater clinic. The patients to be shown, however, must be carefully selected. Only those who exhibit obvious lesions and physical signs visible from a distance should be selected. Cases of this sort are those of infantile paralysis, meningitis, spastic paralysis and idiocy. Other patients suitable for demonstration are those with large livers and spleens or tumors of the kidneys, scurvy and marked rickets. Those with diseases of the lungs or heart, who have few obvious signs and in whose cases the diagnosis depends chiefly on the careful analysis of the physical signs, are less suitable, as are patients with diseases of the kidneys and with diabetes. In such instances, the report of the case can only serve as a text for a clinical lecture. However, this may be made useful. The same qualifications and the same care in preparation are required for an amphitheater clinic as for the didactic lecture. Nothing must be left to chance. The cases must be picked out days or weeks ahead, charts prepared and photographs selected. All tests that are to be made before the students must be rehearsed in advance, so that there cannot be any slips.

VISITS TO THE WARDS WITH SMALL CLASSES

Visits to the wards with small classes are largely a thing of the past. They have been superseded by the supervision of small sections in the wards, with a discussion of the cases after examination has been made by the students. A visit to the wards, however, is of some value to students and is of great value to graduates. The same preparation is required for both visits to the wards and the supervision of sections. No patient should be shown or assigned unless the instructor has made a careful study and examination in advance and is familiar with the history, physical examination and treatment in the case. This means that he must spend several hours with the patient in preparation for the exercise. No one can do justice to himself or to the students by walking around the ward with the intern for five or ten minutes before the exercise and asking the intern what is the matter with the patients. Some can put up a better bluff than others, but no one can do more than bluff. In teaching graduates, however, it is sometimes useful to discuss new patients whom the instructor has not seen, in order to show them how to approach a new case, how to reason about it and how to make the

examination. The instructor not only should examine his patients in advance, but should be as well prepared on the diseases that they have as if he were going to give a lecture. The literature concerning the diseases should have been read. These exercises are much harder to give than either didactic lectures or amphitheater clinics, because the students can ask questions and demand immediate answers. They also make mistakes, and their mistakes must be pointed out to them. The instructor cannot dodge or slur over what he does not know thoroughly, as he can in a lecture. The instructor must think in advance of all the questions, both intelligent and unintelligent, that a half-trained person with a bright mind, who thinks he knows a great deal, can ask, and must be prepared to answer them. He must be as well prepared to show why things are not as the student thinks they are, as to show him what they are. He must be prepared to answer all questions, relevant or irrelevant, and to explain everything in the minutest detail. The visit to the wards and the teaching of sections are the most severe tests of a teacher's knowledge. Nevertheless, these exercises are the ones most often neglected and the ones most often turned over to the junior instructors. They are especially valuable in making the student observe, reason and think for himself.

OUTPATIENT TEACHING

It is impossible for the teacher to make any preparation for outpatient exercises. He must do the best he can with what he knows, and must vary his teaching according to the capacity of the students. As always, he must keep away from his own hobbies and theories. He must be practical, and must remember that the chief object in these exercises is to train the student to think for himself, to cultivate his own powers of observation and to handle the children and parents. The instructor's duty is to guide the student, to point out his mistakes and to show him better methods. Above all, he must set a good example as to carefulness and thoroughness, must never lose his temper either with the students or with the patients, must teach him tact and, if necessary, show him how to act like a gentleman. The outpatient department is the best place in which to teach the student the difference between essentials and nonessentials in diagnosis; that is, how to get on without frills. It is the best place to prepare him for everyday practice. It is the place to teach him how much can be learned from a careful history and a physical examination and to show him what laboratory procedures are necessary and how many of them can be dispensed with in everyday work.

CASE TEACHING

By case teaching, I mean the discussion with the students of the printed record of a case given out at a previous exercise. This type of teaching is especially useful for students in their last year and for gradu-

ates who are general practitioners. For this sort of teaching to be successful, the records of the cases must be carefully prepared in advance, the students must study them in advance and the instructor must be able to arouse the enthusiasm and to keep up the interest of the students. He must be able to put "pep" into the exercise. He should be the leader and merely guide the exercise, making the students discuss the cases themselves. He should not be one of the players, but should act as referee. To do this well requires the same thought and preparation that are necessary for an exercise in the wards. The instructor must be prepared for every contingency and must be ready to answer every unexpected question and to discuss anything and everything that may be suggested to the students by the study of the case.

THE TEACHING OF RESIDENTS, INTERNS AND STUDENTS ASSIGNED TO THE SERVICE

To teach residents, interns and students assigned to the service, the instructor must be a leader. He must teach by example rather than by precept. If he is not prompt, the men under him will not be prompt; if he does not do his work carefully and well, they will not. If he is not considerate of the patients, they will not be. Not only must he do his own work as it should be done, but he must also see that those under him do their work in the same way. He must be enthusiastic in his work and able to inspire others with his own enthusiasm. He must be able to make others work, but he must also be able to make them enjoy their work. He must have the ability to turn over to others all the work that they are competent to do and to so train them that their competence constantly increases. He must teach not only by example, but also by friendly criticism and discussion. Mistakes due to lack of experience or to excusable ignorance should be pointed out and condoned. Those due to carelessness or to laziness should not be overlooked, and the students making them should be severely reprimanded. Good work, especially if done outside the regular routine, should be recognized and praised. The students must be encouraged to think for themselves and to study and work up their case reports by themselves. Their arguments and conclusions must always be given proper consideration, even if they are wrong, because discussion and review proving them wrong often teach them more than getting it right themselves. Finally, the chief must always be courteous, considerate and fair. He must never demand more than is reasonable, but must insist that what he demands is done.

CONCLUSIONS

To teach well, the instructor must like to teach, must know his subject thoroughly and must be able to think clearly. More than this, he must be able to express himself clearly. He must be interested and

enthusiastic. He must be willing to sacrifice his other interests for his teaching. He must be willing to take the time to prepare himself properly for every exercise. He must be able to inspire the students to think and to work for themselves. He must accept the fact that the financial returns from his teaching will be meager. His reward will consist of the satisfaction of knowing that he has done well a job that he likes.

DISCUSSION

DR. JOSEPH BRENNEMANN, Chicago: There are one or two things in Dr. Morse's paper on which I should like especially to comment. It is perhaps because Dr. Morse and I both date from an older period and are perhaps getting conservative, but I still have a strong belief that an amphitheater clinic is valuable. I would rather sit as a postgraduate in an amphitheater and listen to Dr. Morse describe a case than to go and work up a case report in a ward and have some third assistant go over the case with me. Is not that scientific work? Does not experience that has taken years to acquire amount to more than information acquired in any other way? One could not imagine Dr. Morse, for instance, holding a clinic with four or five students. There is not the inspiration that there is with a larger number of students. I think that the amphitheater clinic is still exceedingly valuable, and I should hate to see it discontinued.

DR. M. L. TURNER, Des Moines, Iowa: Teachers should always remember that they should speak so distinctly that the student does not have to strain to hear.

News and Comment

FEELINGS AND EMOTIONS IN EDUCATIONAL PROCEDURES

At Wittenberg College, Springfield, Ohio, October 19 to 22, a meeting was held to discuss "Feelings and Emotions in Educational Procedures." Dr. M. L. Reymert acted as chairman, and many nationally and internationally known psychologists and physiologists discussed various phases of the subject.

DEATH OF PROFESSOR KIRMISSON

Professor Kirmisson recently died in France. He retired from active work many years ago. He previously had held the position of professor of clinical surgery for children and of orthopedics in the Faculty of Medicine at Paris. His best known work was probably that on congenital deformities.

INCREASE IN PRICE OF THE AMERICAN JOURNAL OF DISEASES OF CHILDREN

Beginning with volume 35 (January, 1928), the subscription price of the AMERICAN JOURNAL OF DISEASES OF CHILDREN will be increased to $5.00 a year, in accordance with the action taken by the Board of Trustees of the American Medical Association at a meeting held on Sept. 9, 1927.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

NEWER HEMATOLOGIC ASPECTS OF THE NEUTROPHILS IN INFECTIONS. ARTHUR WEISS, Am. J. M. Sc. **174**:45 (July) 1927.

Weiss reviews the progress of hematology during the past half century and gives the details of Arneth's study of the morphology of the leukocytes. After employing this classification with its eighty-one subdivisions, the author was unable to find any definite value in the lymphocytic and monocytic subclasses. He also found that a count according to the original classification took forty-five minutes, but that to make a differential count and to use only the subdivision of the neutrophils took twenty minutes. Weiss says that of the men who applied and studied Arneth's scheme thoroughly, Schilling was able to do it in less time, and his results were just as valuable. Schilling found that the segmented forms could all be included under this one heading, but he subdivided the nonsegmented forms into the metamyelocyte of Pappenheim, and the jungkernige and the stabkernige, the staff or rod forms. Thus, only 100 need be counted. The Arneth count took twenty minutes, and this one takes only five. Weiss desired to determine definitely whether or not Schilling's modification of the Arneth classification was superior to the method now universally used and employed this method in his hematologic laboratory. He has gathered information from 1,000 consecutive examinations of blood done at the hospital. In all the examinations, the morphology of the leukocytes was minutely studied. His various charts taken from cases to demonstrate the observations and also case reports show a number of conditions that are accompanied by moderate or severe stimulation of leukocytic formation and demonstrate that a prolonged elevation of the staff count signifies a poor prognosis. In pneumonia, the peak of the chart of the immature cells coincides with the period of crisis, and if the patient passes into convalescence without complications one can watch the unripe forms drop to normal level. The patients who develop an exceedingly high staff count in from the second to the fourth day of pneumonia rarely survive. He states that, with comparatively few exceptions, in cases in which young cells rose to about 50 per cent the prognosis was invariably fatal. His results also show the value of the count in differential diagnosis. It makes little difference whether the total count is 20 or 15 thousand leukocytes, but interest centers in one of three points. Is there a leukocytosis, normoleukocytosis or leukopenia? The former view that a hyperleukocytosis means good resistance and a leukopenia poor resistance in no longer tenable. He believes that the number of leukocytes sent into the blood stream by the bone marrow is dependent on the type of the bacterial toxin and the reaction of the bone marrow to it. After knowing whether one is dealing with hyperleukocytosis, normoleukocytosis or hypoleukocytosis, the next and most important item is: What is the character of the individual cells? He believes that by a careful study the significance of the blood counts will be recognized and when interpreted in conjunction with the clinical picture much information of value will be gleaned therefrom. In surgical cases a high staff count acts more or less like an indicator of pus. During postoperative care, a high count means that all is not well, and that some complication or residual abscess is present. In medical cases, a rise of the staff count after it has begun to drop or a steady high level means a complication. Bronchitis

with a high staff count is most often tuberculous. Weiss also believes that there is a large percentage of error encountered in consecutive leukocyte counts, and consequently the percentage of staff forms is of more value and a chart of the immature cells often coincides more accurately with the course of the illness than the temperature.

J. A. HENSKE, Omaha.

MINERAL SALT CONTENT OF THE BLOOD IN DISEASE. A. S. BLUMGARTEN and GEORGE L. ROHDENBURG, Arch. Int. Med. **39**:372 (March) 1927.

Blumgarten and Rohdenburg describe an investigation primarily undertaken as a clinical application of the work of Rohdenburg and Krehbiel on the effect of the removal of the ductless glands in rats on the salt content of the blood. Due to the observation during the course of the investigation that the relationship between the salt content of the blood and the disturbances of the ductless glands was not constant, the work was extended to include all the clinical conditions at the disposal of medical service at Lenox Hill Hospital, which totaled 173 cases.

The authors believe that this is the first series of cases in which all the determinations of salt content were made on the same patient, in which the blood of each patient of the series was analyzed and the sodium, potassium, calcium, magnesium, chloride and total salt content determined. The authors state that their work attempted to establish the following facts: (1) the average normal figures for each mineral constituent; (2) the average figures for the total amount of salts; (3) the relation of the figures obtained for each salt to the percentage which this constitutes of the total salt content; (4) the relation of the various salts to one another, for example, the relation of the sodium content to the potassium content, and the magnesium to the calcium content, and (5) the absolute and percentage content of the various salts and their relation to one another in various diseases.

The author gives a résumé of the determinations of each of the salts, the percentage of mineral salts, and the relation of absolute figures and those of percentage. He also gives pathologic observations and divides them into three groups: an analysis of diseases associated with minimum figures, diseases associated with maximum figures, and the mineral salt content in specific diseases. These are all detailed concisely — the former in a definite manner and the latter in a comprehensive, detailed table.

The summary and conclusions are given as follows:

1. The mineral salt content of the blood was studied in 173 patients suffering from various diseases.

2. The determinations were made on whole blood, both the absolute and the percentage figures being determined, as well as the total salt content.

3. The normal figures for the various salts were as follows:

Absolute	Percentage
Sodium, from 120 to 180 mg. per hundred cubic centimeters	From 40 to 55
Potassium, from 130 to 170 mg. per hundred cubic centimeters	From 35 to 45
Calcium, from 6 to 11 mg. per hundred cubic centimeters	From 2 to 3
Magnesium, from 2.98 to 4 mg. per hundred cubic centimeters	From 1 to 1.5
Total salts, from 250 to 300 mg. per hundred cubic centimeters.	

4. There is no variation between the absolute salt content and its percentage of the total salts.

5. A reciprocal relationship between the sodium and the potassium content of the blood was determined.

6. The calcium and the magnesium content of the blood usually ran parallel.

7. The most striking pathologic conditions in which a disturbance of the mineral salts in the blood was determined were carcinoma, leukemia and purpura hemorrhagica.

8. In carcinoma there was a strikingly low magnesium content and a low calcium content in 50 per cent of the cases, but not so marked a tendency toward hypermineralization.

9. In two of the cases of leukemia and purpura hemorrhagica that were studied, there was a marked reduction in the potassium content and a compensatory increase in the sodium and the calcium content, which the authors believed was probably due to hemorrhage.

10. A large amount of magnesium was found in the blood of persons with arteriosclerosis and other conditions usually associated with advancing years.

11. In persons who had chronic nephritis with hypertension, the blood showed a low calcium and a high sodium content.

12. In disease of the gallbladder, the total salt and the magnesium content were high.

13. There were a number of tendencies toward changes in the proportion of various mineral substances in other diseases, but the authors did not believe that they were sufficiently striking to be significant. LOEBER, New Orleans.

THE DICK TEST. J. SMITH, Arch. Dis. Childhood **2**:166 (June) 1927.

In sixty cases, certain persons gave negative or slightly positive reactions to the Dick test and were carriers of hemolytic streptococci capable of producing a true exotoxin which could be neutralized by a horse scarlet fever antitoxin.

THE DREYER AND WARD SIGMA REACTION IN CONGENITAL SYPHILIS. HUGO HALL and F. M. B. ALLEN, Arch. Dis. Childhood **2**:171 (June) 1927.

Fifty-two cases of congenital syphilis have been tested. All cases showed a definitely positive Sigma reading and also a positive Wassermann (Harrison and Fleming methods) reaction.

AUTONOMIC NERVOUS SYSTEM IN CHILDREN. A. J. CHURA, Arch. Dis. Childhood **2**:191 (June) 1927.

Children with empty stomachs were studied at rest in bed. The skin was frozen with ethyl chloride. The peripheral leukocyte count was made before and after the procedure. Ten cases of measles and seventeen cases of typhoid showing a leukopenia were studied. In measles, while the rash was first appearing, there was a decrease of 29.5 per cent in leukocytes. When the rash began to fade, irritation of the skin produced an increase. When constriction of the vessels occurs, occasioned by the influence of the sympathetic nerves, the number of leukocytes decreases at the same time, as if the impulses emanating from the irritated state of the parasympathetic system reacts on the leukocytes, causing them to accumulate in the irritated area. The reaction varied in intensity with the capacity of the blood vessels in the region affected. Twelve children with artificial alkalosis and seven with artificial acidosis were examined by this method. In alkalosis, there was a decrease in the peripheral leukocytes and an increase in acidosis.

PETERMAN, Milwaukee.

COAGULABILITY OF THE BLOOD IN CHILDREN. A. BACCICHETTI, Clin. pediat. **9**:183, 1927.

The coagulating power of the blood in children is a fixed and constant coefficient. It is not influenced by digestion or other physiologic functions. The temperature of the body or atmosphere does not exert any effect. The coagulation time is affected by atmospheric temperature, temperature of the body and the amount of blood oxygenation. The coagulating power of the blood in disease was studied. In three cases of typhoid fever, it was normal. In four cases of influenzal and croupous bronchopneumonia, it was increased. In two cases of glomerulonephritis following a streptococcic tonsillitis, it was diminished. In one case of nephrosis with edema, it was increased. In one case of catarrhal jaundice, the coagulating power was normal. One case of tetany with laryngospasm showed a marked diminution. In three cases of rickets, one was normal and two showed an increase. An increase was noted in one case of postdiphtheritic polyneuritis. In one patient convalescing from epidemic cerebrospinal meningitis, the coagulability was diminished. During the course of a purpura hemorragica, the coagulating power was normal; when the patient was completely recovered, it was increased. In ten cases of glandular and scrofulous tuberculosis, five showed an increase and five showed a diminution.

ZAMBARANO, Northville, Mich.

THE ACTION OF ULTRAVIOLET RAYS ON THE BLOOD SUGAR IN CHILDREN. UMBERTO FERRI, Riv. di clin. pediat. **25**:217, 1927.

The subjects of this investigation were patients in the hospital who were from 4 months to 6 years of age. The blood sugar was determined before and at thirty minute intervals after the children had been exposed to ultraviolet rays from a quartz mercury lamp.

Irradiation of minor intensity tended to make the blood sugar less than in the control periods; more intensive irradiation, however, increased the blood sugar.

Following the subcutaneous injections of epinephrine, the blood sugar rose more quickly and to a higher figure if the child was irradiated.

In alimentary glycemia, the effect of irradiation varied with the individual child.

HIGGINS, Cincinnati.

Nutrition

DIFFERENCES IN THE BEHAVIOUR OF RAW, PASTEURIZED, BOILED, EVAPORATED AND DRIED MILK ON THE HYDROGEN ION CONCENTRATION OF THE STOMACH. ANGELIA M. COURTNEY, Canad. M. A. J. **17**:919, 1927.

The various forms of milk were studied after being acidified to the normal acidity of the gastric juice. The hydrogen ion concentration of the contents of the stomach of infants under different types of food, as found by Dr. Marriott, was taken as a starting point. This ranged from p_H 3.75 in breast-fed infants to p_H 5.3 in normal infants fed on cow's milk when they were unaccustomed to it.

The main difference found among the different forms of milk was the character of the casein curd. Evaporated milk gave a bulky fluid curd; milk, dried by the roller process, a compact, cheesy curd, and fresh milk, raw, pasteurized and boiled, and milk dried by the spray process, a curd with characteristics between those of the other two groups. There was some difference in the soluble calcium and protein content.

MOORE, Omaha.

RICKETS IN LIVERPOOL. R. AIDIN, Arch. Dis. Childhood **2**:155 (June) 1927.

Aidin states that almost all infants of the hospital class in Liverpool show unmistakable signs of early rickets. Breast-feeding was no preventive. He did not observe any case of craniotobes or sweating of the head; no cases of tetany developed. Rickets was found frequently in marantic infants, and catarrhal complications were no more frequent than in other children. There was no roentgenologic evidence of rickets in infants under 1 year; no tenderness of the limbs was present.

A SUBSTITUTE FOR BUTTERMILK. KENNETH TALLERMAN, Arch. Dis. Childhood **2**:160 (June) 1927.

There is no satisfactory explanation of the value of acid milk mixtures. A new method of preparation of acid milk is offered. Lactic acid is added to dried skimmed milk powder.

GLUTEAL WASTING IN CELIAC DISEASE. REGINALD MILLER, Arch. Dis. Childhood **2**:189 (June) 1927.

A disproportionate degree of wasting of the gluteal region is described in celiac disease.

PETERMAN, Milwaukee.

THE PREPONDERANT RÔLE OF HYPOTHREPSIA IN THE GENESIS OF CHOLERA INFANTUM. L. BYTEK, Rev. franç. de Pediat. **3**:297, 1927.

The author cites thirty-nine cases in which a choleriform diarrhea has been preceded by a condition of hypothrepsia or athrepsia. There also seems to be a corresponding decrease in the frequency of cholera infantum in institutions in which improved methods of feeding have prevented the occurrence of hypothrepsia.

LESLIE, Chicago.

STRONTIUM LACTATE IN RICKETS. A. PAGANI, Clin. pediat. **9**:207, 1927.

Strontium lactate was used over a period of forty days in the treatment of thirteen patients with rickets. No marked changes in the skeleton were noted following its use. The drug was well tolerated, and no toxic effects were observed.

ZAMBARANO, Northville, Mich.

THE INFLUENCE OF PREGNANCY ON TEETH. G. TOVERUD, Norsk. Mag. f. Lægevidensk. **88**:169, 1927.

By experiments on rats given a diet deficient in calcium and vitamin during pregnancy, the author has found a disturbance in the calcium, phosphorus and magnesium content of the constantly growing teeth. These experiments point to the fact that the diet during pregnancy is the controlling factor in the increased disposition to dental caries during this period of a woman's life.

According to the author, the most common deficiency of the diet is lack of calcium and vitamin A.

STUDIES ON THE CALCIUM AND PHOSPHORUS METABOLISM IN EXPERIMENTAL RICKETS IN PUPPIES. T. SKAAR, Norsk. Mag. f. Lægevidensk. **88**:665, 1927.

From the experiments on puppies, the author draws the conclusion that he is dealing with two forms of rachitic processes: One form in which the calcium metabolism seems to be affected primarily; another in which the phosphorus metabolism is the first to suffer.

If disodium acid phosphate is added to the rachitic diet in an amount of 0.1733 Gm. of phosphorus per twenty-four hours, the pathologic condition is highly aggravated. The clinical symptoms in the form of changes in the bones are greatly pronounced. The calcium content of the blood serum is lowered to 50 per cent of the normal value. Both the calcium and the phosphorus balance is negative.

TOVERUD, Oslo.

Prenatal Conditions

UNUSUAL CASE OF CONGENITAL COXA VARA. H. A. T. FAIRBANK, Proc. Roy. Soc. Med. **20**:237 (Jan.) 1927.

The patient was a boy, aged 3¼ years. At the age of 4 days, it was noticed that the right leg was short, and at that time it was thought to be due to fracture at birth. At 8 months, the shortening amounted to 2½ inches (6.2 cm.); at 3½ years, to 4½ inches (10.2 cm.). The shortening was confined to the thigh. The great trochanter on the right side was markedly raised, with limitation of abduction and internal rotation.

Roentgenograms show that the right femur was short and dense, and curved in its upper third with a clear interval over 1 inch (2.5 cm.) in width between the trochanteric region and the ossific center for the head. Extension was applied, but without a good result. It was proposed to perform an osteotomy on the femur to correct some of the deformity. It was presumed that the neck of the femur was present but unossified. At a later meeting, it was reported that the child died suddenly at operation. Death was due to pulmonary thrombosis. It was found that the neck of the femur was present though cartilaginous.

BONY ANKYLOSIS OF INTERPHALANGEAL JOINT OF FINGER. B. WHITCHWICH HOWELL, Proc. Roy. Soc. Med. **20**:239, 1927.

Dr. Howell reported a case of bony ankylosis of the interphalangeal joint of a finger in a girl, aged 12 years. There had been sloughing of the extensor tendon and osteomyelitis of the first and second phalanges following application of phenol for warts. The joint had been involved. It was put up in a splint in extension until ankylosis took place. The treatment proposed was excision of the ankylosed phalanges and reunion in such a way that the last interphalangeal joint would take up the position of the first when the fist is closed. The extensor tendon was sutured.

SCAPHOID TUMOR: A CASE FOR DIAGNOSIS. A. ROEYN JONES, Proc. Roy. Soc. Med. **20**:240, 1927.

Dr. Jones reported a case of scaphoid tumor. The patient, aged 4 years and 11 months, was brought to the hospital on account of swelling on the inner side of the left foot, which had grown gradually during the past nine months. Roentgenograms showed all tarsal bones present and of normal appearance except the scaphoid, which was represented by a large, irregular mass composed of four segments fused together. It was suggested that the swelling might be a chondroma, although there were no lumps on any of the other palpable bones; or it might be an irregular overgrowth due to trauma. There was no history of injury.

TWO CASES OF HYPERTELORISM. W. G. WYLLIE, Proc. Roy. Soc. Med. **20**:324 (Feb.) 1927.

Hypertelorism is a faciocranial deformity in which the great wings of the sphenoid are abnormally small and the lesser wings large. Through this

deformity, the eye sockets become widely separated and the nasal cavities broadened. One patient, aged 4 years, showed this deformity, while his twin brother had a normal facies. His sister, aged 2 years, showed similar facial deformities. The father and his seven brothers and sisters showed the same deformity, and one of his sisters' daughters had the same peculiarity. All were healthy and normal mentally.

WILLIAMSON, New Orleans.

PETIT'S EVENTRATIO DIAPHRAGMATICA. C. BLAXLAND LEVICK, Proc. Roy. Soc. Med. **20**:51 (July) 1927.

Levick describes a girl, aged 5. This case appeared to be the first of right-sided eventration to be recorded in this country. It was practically identical, clinically and roentgenologically, with one that was described by Bayne Jones in which the diagnosis was confirmed by operation.

DEFORMITY OF RIGHT SHOULDER, WITH ASSOCIATED DEFORMITIES OF RIBS AND CERVICAL SPINE. W. E. TANNER, Proc. Roy. Soc. Med. **20**:194, 1927.

Dr. Tanner reported a case of deformity of the right shoulder, with associated deformities of the ribs and cervical spine in a school girl, aged 13 years.

WILLIAMSON, New Orleans.

Diseases of the New-Born

OBSERVATIONS ON THE PARIETAL FONTANELLE IN THE NEW-BORN AND IN YOUNG INFANTS. F. L. ADAIR and R. E. SCAMMON, Am. J. Obst. & Gynec. **14**:149, 1927.

Results are given on the study of 598 living new-born infants and children of the first and second years.

The fontanels were traced on a strip of closely woven linen cloth held tightly over the cranial vault. The records were completed by noting the infant's age, sex, weight and length.

A definite enlargement of the parietal portion of the sagittal suture was noted in 104 of the 598 cases. All of these were observed in the first 90 days of life. Thirty and seven-tenths per cent occurred in the first month, 27.8 per cent in the second, and in the third, 13.3 per cent.

These figures include all enlargements. If those under 1 sq. cm. are excluded, it cuts the total number to eighteen.

The parietal fontanel is usually located at the level of the parietal eminences.

From the tracings studied, the authors believe that some of the parietal fontanels have their origin from duplications of the centers of parietal ossification. A number, however, seem to be formed from posterior extensions of the great fontanel and a few from forward extensions of the occipital fontanel.

A STUDY OF THE INFANT'S BIRTH WEIGHT AND THE MOTHER'S GAIN DURING PREGNANCY. J. M. SLEMONS and R. H. FAGAN, Am. J. Obst. & Gynec. **14**:159, 1927.

The authors feel that the maternal diet should be regulated to insure only that gain in weight which can be attributed to the growth of the fetus and uterus; this is usually about 15 pounds (6.8 Kg.). This can be accomplished on a diet of about 2,000 calories a day. They were able in a series of 500 cases to obtain an average of a maternal gain in weight of 16½ pounds (7.2 Kg.) and an average fetal weight of 7¼ pounds (3.3 Kg.) on this diet.

The authors conclude that the infant's weight cannot be definitely controlled by maternal diet. However, in general, the mothers that gained in weight during pregnancy gave birth to the largest infants.

THE SIGNIFICANCE OF INFLAMMATION OF THE UMBILICAL CORD. R. S. SIDDALL, Am. J. Obst. & Gynec. **14**:192, 1927.

In 1,000 consecutive cases studied between the seven lunar months and term, inflammation of the cord was found microscopically in sixty patients.

Maternal syphilis was known to be present in only one of these cases. In the majority, however, there was evidence that pointed to bacterial infection such as premature rupture of the membranes — intrapartum elevation of temperature and leukocytic infiltration of the placental amnion and chorion.

The authors found that the prognosis of the condition of the child was not affected.

ALLEN, Chicago.

A CASE OF SO-CALLED WINCKEL'S DISEASE (CYANOSIS AFEBRILIS ICTERICA CUM HAEMOGLOBINURIA). WILLIAM FELDMAN, Brit. J. Child. Dis. **24**:113 (April-June) 1927.

The first description of the disease was given independently in 1873 by Laroyenne and by S. Charrin, who described an epidemic of thirteen cases as "maladie bronzée hématique." In 1874, Bigelow described an epidemic of ten cases at the Boston Lying-in Hospital; eight of these patients died. F. Winckel published his description in 1879, based on an epidemic of twenty-three cases at the Dresden Lying-in Hospital.

The onset of the disease occurs during the first few days of life, most frequently on the fourth, when the infant begins to look blue all over the body. When the most cyanotic places are scratched, some viscid, chocolate colored blood can be squeezed out. Cyanosis is soon followed by jaundice of different degrees of intensity, and the pulse and respiration are accelerated and hemoglobinuria appears in all cases. The infant becomes lethargic and except in mild cases death occurs within two or three days. At postmortem examination, the renal cortex is usually found to be broader than normal and contains multiple hemorrhages, and the pyramids contain hemoglobin infarcts. Hemorrhages are also found in the pleura, pericardium and heart muscle. The causal organism of the disease has not been found.

The author's report of the case of a boy, first seen at the age of 4 days, who died on the seventh day, fits in with the clinical description of the disease. The results of the autopsy were, however, entirely negative.

LANGMANN, New York.

COMPARISON OF THE BODY MEASUREMENTS OF THE NEW-BORN OF TREVISO AND THE NEW-BORN OF PADUA. GAETANO SALVIOLI and LEOLIA MEAGLIA, Riv. di clin. pediat. **25**:498, 1927.

Treviso and Padua are neighboring provinces. Anthropologic measurements were made of 100 new-born infants from each place. No appreciable differences were found. One might expect more difference in such a study if one grouped according to racial characteristics instead of according to geographic location.

HIGGINS, Cincinnati.

Chronic Infections

HEREDITARY SYPHILIS AND THE ENDOCRINE SYSTEM. L. BABONNEIX, Arch. de méd. d. enf. **30**:201, 1927.

Prof. Hutinel, in 1918, first brought the attention of the medical profession to the relation between glandular syndromes, both single and multiple, and inherited syphilis. In a series of articles published since then, he has endeavored to strengthen his contention that the dystrophies of infancy are practically always due to the effects of syphilis of the ductless glands.

This hypothesis was vigorously attacked by Nicolas and Gaté at the recent Congress of Dermatology and Syphilis, held in Brussels. In favor of Hutinel's theory, Babonneix assembles the following arguments:

1. In hereditary syphilis, spirochetes may be found in great numbers in many of the endocrine glands. This is particularly true of the suprarenals, the pancreas, the thyroid and the gonads.

2. In the dystrophies of childhood, the Wassermann reaction is often positive, either spontaneously or through reactivation.

3. In postmortem examination in cases of hereditary syphilis one finds syphilitic lesions not only in the liver and spleen, but in the suprarenals, the parathyroids and the hypophysis.

4. On the clinical side, it has been shown that many forms of infantile dystrophy, either partial or general, are associated with heredosyphilis, as are also, at times, the developmental errors seen in eventration, anencephaly, syndactylism, spinal bifida, meningocele, etc. Idiocy, gigantism, achondroplasia, infantilism and obesity of congenital origin may be due to syphilitic pluriglandular involvement.

AMESSE, Denver.

RESEARCHES ON THE BONY DISTURBANCES IN THE CONGENITAL SYPHILIS OF INFANCY. M. PEHU and A. POLICARD, Rev. franç. de pédiat. **3**:137, 1927.

In a recent survey of sixty-seven infants with congenital syphilis, forty-three showed periostitis ossificans. An intensive study was made of ten cases, some of which came to autopsy. The authors feel that the process is essentially one of rarefaction with formation of new bone. This accounts for the successive layers of periosteum visible in the roentgenogram. It is suggested that the term syphilitic hypertrophic osteoporosis corresponds more closely to the histopathologic picture than the more frequently used term of syphilitic periostitis ossificans.

INFLUENCE OF ULTRAVIOLET RAYS ON CUTANEOUS SENSITIVITY TO TUBERCULIN. P. WORINGER and A. ADNOT, Rev. franç. de pédiat. **3**:204, 1927.

Tuberculous subjects who showed definitely positive Pirquet tests were used in this study. One half of the body, always the same half, was exposed repeatedly to ultraviolet light. Bilateral Pirquet tests were made from time to time. It was found that the reaction became definitely less on the exposed side as the exposures continued. The authors conclude that ultraviolet rays diminish the sensitivity of the skin to tuberculin, and that their effect is limited to the exposed area and does not extend to the rest of the skin.

Keeping in mind the therapeutic value of ultraviolet light, it would seem that no parallelism exists between allergy as shown in cutaneous sensitivity and immunity as evidenced by resistance to the infection. LESLIE, Chicago.

Internal Diseases

CARCINOMA OF THE CERVIX IN A THIRTEEN YEAR OLD PATIENT. ADOLPH BONNER, Am. J. Obst. & Gynec. **14**:175, 1927.

This case report of a Jewess, aged 13, who had adenocarcinoma of the cervix, brings forcibly to one's attention that all cases of vulvovaginitis and irregular vaginal bleeding demand an examination with the speculum. A diagnosis of traumatic vulvitis was made, although no history of trauma was obtained, and the patient was treated on this basis for several months.

Treatment with the roentgen ray and radium was instituted, and the patient is still well nineteen months after the first operation. ALLEN, Chicago.

FRAGILITAS OSSIUM AND DEAFNESS. JOHN J. SHUGRUE; REED ROCKWOOD, and EDWARD W. ANDERSON, Arch. Int. Med. **39**:98 (Jan.) 1927.

Four cases of blue sclerotics, brittle bones and deafness are reported. The cases are characterized by blue sclerotics, early and continued occurrence of fracture, because of the fragile type of the bones and sometimes the development in early youth of progressive deafness.

The disease is hereditary, and a patient may have one, two or all symptoms. Children afflicted with blue sclerotics alone usually die in infancy. When the blue sclerotics are first manifest in adolescence, they are associated with brittle bones, and later deafness may supervene.

A review of the literature shows only thirty-eight reported cases in America.

In the four cases given by the authors, the source of these groups seems to be from Europe. Again two of the four cases are definitely hereditary, while the other two reveal no familial tendency. They believe that one of their cases definitely follows the mendelian law. In all reported cases the sclerotics were uniform. No matter in which direction the eyeball was turned, the homogeneous leaden blue was seen through the scleral conjunctiva. It is variously described as porcelain or leaden blue.

The fractures may be spontaneous or associated with trauma.

The relation of the syndrome of blue sclerotics and brittle bones to the condition known as fragilitas ossium, osteogenesis imperfecta and osteopsathyrosis, is unknown. It is noteworthy that many authors writing on these diseases make no mention of color in the sclerotics nor of hereditary tendencies. The accompanying deafness seems to be due to otosclerosis, a lesion of the auditory nerve. The most plausible explanation for the blue sclerotics as well as the brittle bones and deafness is that they are caused by a congenital mesenchymal defect, since all the structures involved in the syndrome come originally from this anlage. However, this theory does not explain why other tissues of mesenchymal origin, such as the heart, the blood and lymph vessels, the bone marrow and the lymph nodes, are not usually affected. Little is known of the metabolism of inorganic salts in these cases. Like Flagstad, Zanger and Levin, the authors have found normal values for serum calcium and inorganic phosphorus. The authors conclude with the statement: "The disease is uncommon. It is progressive although concomitant with longevity." The ages of the four patients cited are 20 years, 47 years, 49 years and 52 years, respectively, the first two men and the last two women.

HYPERTENSION IN PREGNANCY: RELATION OF THE CALCIUM CONTENT OF THE BLOOD TO THE ETIOLOGY. EDWARD J. STIEGLITZ, Arch. Int. Med. **39**:465 (April) 1927.

After reviewing the literature on the subject, the author says: "Evidence has been presented which indicates that a metabolic disturbance associated

with a hypocalcemia may be one etiologic factor in hypertension and in other conditions of increased smooth muscle tonus. If this is the case, the hypocalcemia should be most conspicuously manifest in the hypertensions of pregnancy, in which condition a maternal depletion of calcium takes place. That the parathyroid glands are intimately associated with calcium metabolism is clearly demonstrable. A relatively comprehensive objective study of the blood pressure and blood calcium determinations in a series of pregnant women was therefore undertaken to determine, if possible, any relationship between the two phenomena."

The present investigation deals with the results obtained in 222 determinations of blood calcium from a series of cases, including normal pregnant patients, pregnant patients showing hypertension, and also some nonpregnant controls. The method used is outlined, the grouping of the cases of hypertension classified into four divisions and the results arrived at are summarized as follows by the author:

Hypocalcemia is not of major etiologic significance in arterial hypertension in pregnancy, despite the fact that in such cases the relationship should be most conspicuous.

During the final month of pregnancy, a gradual rise in arterial tension is associated with a moderate hypocalcemia.

Immediately after parturition a fall in blood pressure occurs, with a corresponding rise in the concentration of blood calcium.

Coincident and probably associated with the onset of lactation, a secondary elevation in arterial tension occurs, with a corresponding and equally transient hypocalcemia.

The latter phenomenon permits of physiologic interpretation.

HODGKIN'S DISEASE, WITH PREDOMINANT LOCALIZATION IN THE NERVOUS SYSTEM; EARLY DIAGNOSIS AND RADIOTHERAPY. SOLOMON GINSBURG, Arch. Int. Med. **39**:571 (April) 1927.

The author takes exception to the original definition of Hodgkin's disease as an "affection of the absorbent glands and spleen"; he reviews the literature and gives in detail ten cases of his own to uphold his views, particularly those on the invasion of the nervous system. He scores history taking as it is practiced in a large hospital service and blames the loose method in which it is done for the failure of these cases to come to an early, correct diagnosis. In his concluding remarks, he says:

"Hodgkin's disease should no longer be defined as a specific enlargement of the lymph glands and spleen with occasional deposits in other viscera accompanied by a severe secondary anemia. It is a specific malignant general disease with protean manifestations in which any tissue or organ in any region of the body may become clinically, primarily and predominantly affected. Pathologically, Hodgkin's disease is characterized by a special hyperplasia of the reticulo-endothelial elements wherever the invasion of the morbific agent or process occurs.

"The invasion of the nervous system in Hodgkin's disease is by no means as rare as textbooks would lead one to believe.

"Early diagnosis of Hodgkin's disease of the nervous system can be made only on the basis of a thorough and complete study of all the clinical signs and symptoms present in a given case. A neurologic examination alone, supplemented even by various laboratory tests directed exclusively toward the nervous system, may prove insufficient to establish a diagnosis. In doubtful cases, therefore, the radiotherapeutic test may prove an important aid in diagnosis."

Radiotherapy, which is the chief measure in the treatment of this malignant disease, must be used early, for in the late fibrotic stages its efficacy is nil. When used early and effectively, it may relieve a paraplegia that may never recur.

PRESENT STATUS OF CURABILITY OF BRONCHIAL ASTHMA, WITH REPLIES TO A QUESTIONNAIRE. MORRIS H. KAHN, Arch. Int. Med. **39**:621 (May) 1927.

The author begins his thesis with the following paragraph:

"Reports of the benefit derived from the methods of treatment of bronchial asthma are extremely diverse and often depend on the enthusiastic preconceptions of the physician, the psychic susceptibilities of the patient and the spontaneous tendency of the disease to remissions, aggravations and improvement."

He then proceeds to quote from forty-eight medical articles, one antedating 1910; and for every theory and fact observed by the particular authority quoted, a counter theory and the opposite experimental fact was quoted and contradicted the foregoing statements. As the author tersely says, "This profusion of articles has added voluminously to the literature on the subject, advancing the science of it but little."

The same treatment is accorded the relation of the nose and metabolism to asthma as well as the alleged "cure" of asthma. In regard to the latter, he specifically says, in referring to answers that he received in reply to an inquiry on the curability of bronchial asthma sent out to the workers most prominent in this field in the United States, that it will be seen that opinions range from the belief that an absolute, permanent cure in asthma is unobtainable (Gottlieb) to an assertion of 100 per cent of cures in pollen cases (Duke). He elucidates this 100 per cent of cures in pollen cases by adding, in his letter as in his writing, Duke uses the term "cure" but not in the sense of complete or absolute cure in which the patient does not require any further treatment. He says that a rather large proportion of persons inherit a constitution which makes it possible for them to become hypersensitive to foreign substances. Once sensitive, they are likely to react in characteristic ways whenever they come in intimate contact with the substances to which they are sensitive.

The author states frankly and boldly his position: "The term 'cure' is definite in its significance. It means to heal, to restore to sound health, to subdue or remove an ailment by remedial means. A method of treatment or a medicine cannot be held to be a cure if it does not entirely eliminate the disease from the body. We do not speak of a cure of Hodgkin's disease, or of cancer, or of diabetes mellitus unless the pathologic background of the condition is effaced and the person continues to maintain normal health without further treatment. It is in this way that we must apply the term 'cure' to bronchial asthma. And, thus far, by all the methods that have been created, a cure has not been discovered."

Concerning heredity in bronchial asthma, the importance of constitutional predisposition and the conspicuousness of the family tendency in this disease has long been recognized.

After more references and some discussion, the author reaches the conclusion, "The final solution in discovering the genesis of bronchial asthma lies in the phenomena of heredity" and ends his paper with the following concise summary and conclusions.

Summary.—Reports of the benefit derived from the various methods of treatment of bronchial asthma are extremely diverse. Thus far, no method of

treatment seems to have greatly influenced the course of the disease, which is naturally variable.

In its etiology, anaphylaxis may be dismissed from consideration. Protein sensitization is indeed a phenomenon in this disease, but it apparently is not the basic cause of the condition. It is true that the sensitization tests indicate intoxication by some substance or substances, usually protein in nature; but treatment for purposes of desensitization or immunization is futile in the endeavor to obtain an absolute cure.

The relation of nasal disease to asthma shows evidence of a constitutional susceptibility rather than a causal relationship, just as do vagotonia, hemoclasic crises and all the other theories thus far advanced as causative of asthma.

The final solution in discovering the genesis of bronchial asthma lies in the phenomena of heredity. The condition is rooted in the biologic and physiochemical structure of the chromosomes. A hereditary factor is present, not in a certain fraction of the cases, but in 100 per cent of the cases. The fallacies of statistics on heredity in man are well established and depend mainly on the insufficient knowledge of ancestry in cases of bronchial asthma.

Conclusions.—An absolute cure of asthma is therefore not to be expected until a method has been found which will alter the chromosomal constitution either in the adult or, more radically, in the genetic cells.

ADDISON'S DISEASE AND DIABETES MELLITUS OCCURRING SIMULTANEOUSLY: REPORT OF A CASE. JOHN H. ARNETT, Arch. Int. Med. **39**:698 (May) 1927.

The author reviews the cases in the literature and states that the combination of diabetes and Addison's disease appears to be of extremely rare occurrence. He then proceeds to give a complete and detailed report of his case.

On several occasions, he calls attention to the fact that the patient showed a hypersensitivity to insulin. This, he says, can best be explained on the basis of diminished suprarenal function and summarized his report as follows:

The combination of Addison's disease and diabetes mellitus is extremely rare. It is, moreover, of great interest, because the two ductless glands involved, namely, the suprarenals and the islands of Langerhans, secrete hormones producing opposite glycemic effects. The case herewith reported presented both the clinical and the chemical evidences of diabetes mellitus, together with the pigmentation, asthenia, low blood pressure and vomiting that are characteristic of Addison's disease. Autopsy bore out this diagnosis. Unusual therapeutic difficulties were encountered, owing to the existence of a hypersensitivity to insulin and a marked tendency to ketosis, the former, no doubt, being due to suprarenal insufficiency.

SEVERE CHRONIC GLOMERULAR NEPHRITIS, WITHOUT HYPERTENSION, CARDIAC HYPERTROPHY OR RETINAL CHANGES: REPORT OF TWO CASES. EDWIN G. BANNICK, Arch. Int. Med. **39**:741 (May) 1927.

The author states that although these unusual cases have been recognized and some of them reported, there is great need of more clinical data in order to study and appreciate better the relationship of hypertension and cardiac hypertrophy to nephritis, a point emphasized by Foster and others. It is for this purpose that the following cases are reported:

In case 1, that of a man, aged 49, the records are complete and permit conclusions to be drawn which are definite enough to give title to this article. In the second case, that of a boy, aged 15, although the patient came to the clinic because of an abscess of the right axilla, anorexia, weakness and malaise,

having had scarlet fever at the age of 9, influenza at 10, tonsillitis at 12, and furunculosis at 13—a significant history—the data are not so complete, and all of the blood pressure readings are not so definitely normal as in case 1. However, the two cases are similar and so unusual that it seems advisable to report both. The cases are given in full, including a protocol for each case.

The author concludes as follows:

"Rare cases of severe chronic glomerular nephritis terminating in uremia may occur without hypertension, cardiac hypertrophy or retinal changes. The appreciation of this possibility aids in the correct diagnosis of these unusual cases and adds important data to the study of hypertension and nephritis."

THE PROTEIN TEST FOR UREA FORMATION FUNCTION OF THE LIVER. PHILIP COHEN AND S. J. LEVIN, Arch. Int. Med. **39**:787 (June) 1927.

The authors review the numerous tests for liver function and state that, whereas one of the most important functions of the liver is the deaminization of amino-acids and their conversion to urea, a standard test for the conversion of urea by the liver has not been elaborated; in fact, this test has largely been neglected.

The present liver tests and their relative values are discussed, and not a few are discounted as unreliable.

The authors' tests were the results of experimentation on sick or convalescing children.

The authors state that for the purpose of this study, cases of obvious injury to the liver were selected, but they also investigated cases in which there was reason to suspect disturbed function of the liver. To check the results, other proved and accepted tests for function of the liver were employed at the same time. The figures of accepted results of these tests were used as standard. A series of control cases showing an apparently normal function of the liver was studied. After various methods were tried, the final procedure was as follows:

1. While the patient was fasting, a specimen of blood was taken in order (*a*) to determine the blood sugar and (*b*) blood urea, (*c*) to make a quantitative determination for bilirubin (the van den Bergh test), and (*d*) to use as standard for dye test.

2. Dye was then injected intravenously. At first the phenoltetrachlorphthalein dye was used, but later the authors used bromsulphalein because venous thrombosis was frequently caused by the first dye, and because of possible deleterious results like those reported in the literature.

3. Blood was withdrawn for determination of the dye in fifteen minutes and in one hour for the phenoltetrachlorphthalein test or in thirty minutes for the bromsulphalein test.

4. Levulose was given, 1.5 Gm. per kilogram. The blood sugar was then determined every half hour for two or three hours.

5. The protein meal was given, 1 Gm. per kilogram, and the blood urea taken four hours later.

6. Twenty-four hours urinalyses were made to determine the amount of urobilin. At first the authors used the Wallace-Diamond test, but later they employed the more satisfactory Joyce test as modified by Kuttner.

In this way all the tests could be performed in one day, and thus easily repeated when changes in the clinical condition occurred. Checks showed that the tests so performed did not interfere with the results.

As a control series, the authors used children who were suffering from a disease that they were clinically certain did not affect the function of the liver.

The effect of a protein meal on the blood urea was studied at two and four hour intervals after the ingestion of the meal, and occasionally six hour studies were made.

From easily tabulated tables are noted the results of the study. Table 1 shows that the maximum increase in blood urea, after a protein meal in children with apparently normal livers, was four hours. Table 2 does not reveal any increase in the blood urea after a glucose meal in children having apparently normal livers.

Table 3 gives results of tests for liver function in children with a definite pathologic condition of the liver as evidenced by jaundice and large liver. The authors call particular attention in this chart to the first case in this series, one of pneumonia which was marked by jaundice and large liver. All tests including the protein test yielded subnormal results, but after the pneumonia had completely resolved, the jaundice disappeared and the liver became normal in size; tests for liver function were normal, including the protein test, which then caused a 50 per cent increase in four hours.

Table 4 represents another group of patients having heart disease who were studied to determine whether the clinical symptoms of an enlarged liver and the commonly encountered subicteric tint were associated with signs of a lowered function of the liver.

The table shows that the van den Bergh and the protein tests give positive results, but the authors discredit the other tests in this group.

A group is studied to ascertain liver function in cases of toxic pneumonia and other group of cases of mild pneumonia. In cases of toxic pneumonia, the protein test for liver function in three of four cases revealed subnormal urea formation of liver. Before the children were discharged from the hospital the protein tests, together with other tests, had become normal, demonstrating to the authors the rapid recovery of the liver in convalescence after pneumonia. Mild forms of pneumonia revealed little change in liver function.

Another group of miscellaneous cases were studied as there was reason to suspect a disturbance of the liver; this group included a case of leukemia, Hodkgin's disease, suspected abdominal tuberculosis, and case of ketosis, and the authors conclude that the most constant and most positive indicator of hepatic hypofunction was the protein test.

The authors' conclusions are:

1. A new test for liver function is described, based on the normal conversion by the liver of amino-acids to urea.

2. After a protein meal of 1 Gm. per kilogram of weight, the blood urea will increase as the blood sugar does after a glucose meal. Normally, the blood urea will increase at least from 50 to 70 per cent above the fasting level in four hours.

3. In cases of injury of the liver, this increase of the blood urea after a protein meal is much diminished, usually below 50 per cent, and sometimes an increase does not result in four hours.

4. Other tests for liver function have corroborated this test of subnormal hepatic function.

5. When the liver again becomes normal, the protein test also causes a normal increase in blood urea.

CEREBROSPINAL FLUID IN NEPHRITIS. JOHN D. LYTTLE and LESTER ROSENBERG, assisted by JOHN E. HEARN, Arch. Int. Med. **39**:808 (June) 1927.

In this paper, it is urged by the authors that it is essential that further work on the examination of the cerebrospinal fluid in apparently noninflammatory

conditions, such as chronic nephritis, for the purpose of studying the increased protein (albumin and globulin) be made with an effort to clarify definite diagnosis in cases simulating the true types of cerebral irritation.

The authors regret that they had only twenty-two cases of nephritis from which to draw conclusions and not many autopsies on which to corroborate these conclusions. A detailed account is given of the methods employed and the results obtained, and a comprehensive table of the twenty-two cases setting forth the results of the tests on the blood and the spinal fluid in nephritis is given.

The following conclusions are arrived at by the authors:

1. Studies of the cerebrospinal fluid and the blood were made in cases of nephritis with and without uremic manifestations.

2. The cerebrospinal fluid in chronic nephritis shows the following:

(*a*) The fluid is clear. This was true in all of our cases except one, in which the fluid had a faint yellow-green tinge. Pressure, as judged by the initial spurt and rapidity of flow, is increased.

(*b*) The cell count varies from 2 to 16 per cubic millimeter; these cells are essentially all lymphocytes. With the exception of one case showing a polymorphonuclear count of 50 per cent, this was true in the series studied. The presence of uremia has no relation to the cell count.

(*c*) The nonprotein nitrogen of the cerebrospinal fluid is increased and is higher than the normal proportion in relation to the blood nonprotein nitrogen. The ratio, $\frac{\text{Cerebrospinal nonprotein nitrogen}}{\text{Blood nonprotein nitrogen}}$, normally 46 per cent, rises to 80 per cent in the presence of nitrogen retention.

(*d*) The chlorides are not generally increased. The figures for the cases showing edema are essentially the same as for those not showing edema. In fluids taken post mortem, the chlorides are exceptionally high.

(*e*) There is a definite increase in albumin and globulin in chronic nephritis; the highest figures are obtained in the presence of uremia. When the protein is more than 100 mg. per hundred cubic centimeters, the prognosis is grave.

(*f*) The ratio, $\frac{\text{Blood sugar}}{\text{Cerebrospinal fluid sugar}}$, is higher in chronic nephritis, averaging 74.3 for eleven of the cases. More than 50 per cent of the cases gave a higher cerebrospinal fluid sugar than normal. In the presence of uremia, the average figure obtained is higher than in the absence of uremia.

3. In the absence of uremic manifestations, the cerebrospinal fluid in acute nephritis is essentially normal in all respects. In the presence of uremic symptoms, the protein content rises.

4. In the acute nephritis of mercuric chloride poisoning, the cerebrospinal fluid resembles closely that seen in chronic nephritis.

5. Apparently there is not a characteristic change in the colloidal gold curve of the cerebrospinal fluid in nephritis. The amount of protein per se, that is, albumin and globulin, bears no direct relation to precipitation of the colloidal gold suspension.

AUDIBILITY OF BRUIT OF THE THYROID IN EXOPHTHALMIC GOITER. ISRAEL BRAM, Arch. Int. Med. **40**:110 (July) 1927.

It is the opinion of the author that the presence of bruit helps to differentiate exophthalmic goiter from toxic adenoma and that in the absence of exophthalmos in an otherwise typical case of exophthalmic goiter, the characteristic bruit of the thyroid is almost pathognomonic. Two methods are

given of altering the audibility of bruit in the hyperplastic thyroid of exophthalmic goiter: (1) through change of the patient's posture, and (2) through the use of iodine.

Two photographs are given to illustrate the first method. Figure 1 shows the usual position of the head extended, chin raised upward and the anterior aspect of the neck made taut. In figure 2, the patient's neck is placed in the flexed position with the chin forward or approaching the chest; in this position, with the stethoscope over the isthmus of the organ (for here the true bruit of the thyroid is obtained rather than the second sound of blood passing through the carotid arteries), a soft bruit becomes loud, a questionable one distinct, and often a thyroid presenting no bruit in the extended position will present one in this posture.

In typical instances the sound is loud and at times uncomfortably harsh to the ear, simulating the bruit heard over an aneurysm; it is systolic, though occasionally diastolic, in time. In this flexed position of the neck with the stethoscope over the isthmus, the author claims to elicit bruit over the thyroid months in advance of the development of marked enlargement of this organ in exophthalmic goiter, thus assisting in the making of an early diagnosis.

In the second method — the discontinuation of the administration of iodine — the author claims results in the disappearance of the excessive colloid accumulation within from ten to twenty days, with the reappearance of the former bruit.

LOEBER, New Orleans.

THE HEART IN CHILDHOOD: CLINICAL OBSERVATIONS. S. CALVIN SMITH, M. J. & Record **126**:28 (July 6) 1927.

There are many characteristics peculiar to the heart in childhood, namely:

1. The heart is more susceptible to damage than at any other age.

2. There are two pulse irregularities known as sinus arrhythmia and sino-auricular block.

3. It is natural for the right side of the heart to be enlarged in the first few weeks after birth.

4. Periapical dental infections rarely derange the child's heart.

5. By far the most frequent source of heart damage in childhood is tonsillar infections. The author advocates tonsillectomy if there is any tonsillar disease, if the child's heart is to be saved for adult usefulness. He also advocates periodic examinations of all hearts that at any time exhibit a murmur, however innocent it may seem.

WILLIAMSON, New Orleans.

MYOCARDIAL DAMAGE IN CORONARY OCCLUSION. JOHN W. SCOTT and JOHN HARVEY, South. M. J. **20**:510, 1927.

The methods and indications for transfusion are discussed. This therapeutic procedure should be done while there is still a good hope for recovery and not as a last resort. Transfusions from citrated blood are preferable in children on account of the ease of performance.

SCHLUTZ, Minneapolis.

ACUTE NEPHRITIS IN CHILDREN. GLADYS L. BOYD, Canad. M. A. J. **17**:894, 1927.

This article is a review of the subject of acute nephritis in children. It is based on observations made on 150 patients with acute nephritis who were admitted to the wards of the Hospital for Sick Children, Toronto, between

1920 and 1926. The author adopted the following simple classification as that most nearly corresponding to the clinical course and the pathologic observations: (1) acute hemorrhagic nephritis, (2) acute tubular or hydremic nephritis, (3) mixed type or acute glomerulotubular nephritis, (4) febrile albuminuria and (5) acute syphilitic nephritis.

While the first type seems to be related definitely to acute infections of streptococcic origin of the upper respiratory tract, this organism was isolated in only a small percentage of cases. In the hydremic cases, careful examination of the nasal sinuses, as suggested by Marriott, resulted in few positive symptoms.

The author feels that the most valuable functional tests are the concentration, water and phenolsulphonphthalein tests.

The determination of creatinine furnishes a more reliable guide in making the prognosis than does any other single constituent of the blood. When blood creatinine does not exceed 4 mg. per hundred cubic centimeters, complete recovery may occur. A progressive lesion is usually present when there are between 4 and 5 mg. present; when more than 5 mg. is found, death occurs within a few months.

The results according to the type of nephritis were:

	Cured, Per Cent	Chronic, Per Cent	Died, Per Cent
Acute hemorrhagic	72	16	12
Acute hydremic	55	21	24
Acute mixed	41	40	19
Acute syphilitic	0	0	100

In the conclusion, Dr. Boyd outlines the treatment of the disease and its complications, which has been considered most satisfactory.

AN EARLY CASE OF CONGENITAL PYLORIC STENOSIS. L. P. MACHAFFIE, Canad. M. A. J. **17**:946 (Aug.) 1927.

A case of true pyloric stenosis, in which diagnosis was made and operation performed thirty-four hours after birth, is reported.

The interesting features of the case, beside the early age at which it occurred, is the method of onset. Fifteen or twenty minutes after birth, the infant became cyanotic. The cyanosis would come on in definite attacks. Each attack would be preceded by gagging. There were no signs of cerebral injury. All fluids were vomited almost at once, with the projectile type of vomiting. Roentgen-ray examination after a barium meal showed no passage of the barium through the pylorus. The operation showed a firm, gristle-like ring, the size and shape of a shelled peanut, encircling the whole of the pyloric ring. The infant made a good recovery.

MOORE, Omaha.

LEUKEMIA IN INFANCY AND EARLY LIFE. G. W. ST. C. RAMSAY, Arch. Dis. Childhood **2**:119 (April) 1927.

One hundred case records of leukemia in children under 8 years were studied, ninety-one of which are taken from the literature. Twice as many cases occurred during the first four years of life as during the subsequent four years. Sixty-two and three tenths per cent were in males. The average duration of the illness was: lymphocytic, 2 months; myelocytic, 4.3 months; lymphoidocytic, 2.1 months. Seventy per cent of the cases were lymphocytic. The symptomatology of the three types was the same.

INDIRECT DETERMINATION OF THE p_H OF THE BLOOD IN CHILDREN. STANLEY GRAHAM and NOAH MORRIS, Arch. Dis. Childhood **2**:138 (April) 1927.

An indirect method of determining the carbon dioxide tension of the arterial blood in children over 2 years of age is described; the determination is made by means of air injected into the rectum. The p_H varies from 7.32 to 7.5 in normal children.

PETERMAN, Milwaukee.

PREVENTION OF RHEUMATIC HEART DISEASE IN CHILDREN. J. F. HALLS DALLY, Brit. J. Child. Dis. **24**:83 (April-June) 1927.

Of 1,200 children in the Wigan district of Lancashire, 29 per cent showed evidences of rheumatism. Modern statistics unite to show the extreme frequency with which carditis is associated with the initial attack of rheumatism. The author stresses the difficulties that surround the early recognition of rheumatism in children, and his impression as to etiology may be gleaned from the following statement: "On the part of those who are not wedded to the infective view as self explanatory there is a consensus of opinion as to certain disposing and evocative factors in rheumatism such as are comprised in the influence of environment in its broadest applications."

LANGMANN, New York.

TWO CASES OF (?) STILL'S DISEASE. W. S. C. COPEMAN, Proc. Roy. Soc. **20**:37 (July) 1927.

CASE 1.—The patient, aged 9, was admitted to the hospital in March, 1925, complaining of pains in the neck, knees and wrists. The wrists were swollen, and there was an urticarial rash over both elbows and on the inner side of the knees. The heart and tonsils were normal. The case was diagnosed as rheumatoid arthritis. The patient was readmitted with the same symptoms in August, 1926. A Flexner bacillus was found in the stools. The patient was seen again, March, 1927; the wrists more swollen, and he was readmitted to the hospital. The Flexner bacillus was not found in the stool. The roentgen ray showed some rarefaction in the carpal bones as well as in the basis of the metacarpals — so-called "drill holes." Flattening of the radial epiphyses, with some sclerosis of the articular surface and appearances typical of Still's disease were noted.

CASE 2.—The patient, aged 6½, had been admitted to the surgical ward of the hospital in July, 1925, for painless swelling of the knees and genu valgum of three years' duration. He had been treated in plaster for fifteen months without any improvement. Operation was performed, June 23, 1925 and only a small quantity of clear fluid was found. A piece of synovial membrane was excised. The fluid in section did not show any pathologic changes. The patient was readmitted, March, 1927, showing the joints to be more swollen; marked "spatula" clubbing of the fingers of both hands, "spatula" clubbing of the toes and a slight tendency to pes valgus were present. Roentgen-ray examination showed: "much joint swelling; no bone changes appearances, not typical of Still's disease but epiphyses of radius and epiphyses at ankles joints are of the type associated with Still's disease."

In both cases, the Wassermann reaction was negative.

A CASE OF ACUTE LYMPHATIC LEUKEMIA. NOEL OLIVER RICHARDS, Proc. Roy. Soc. Med. **20**:49 (July) 1927.

A boy, aged 9, had acute lymphatic leukemia.

CASE OF ANEMIA. R. C. JEWESBURY, Proc. Roy. Soc. Med. **20**:53 (July) 1927.

The author reported a case of anemia because it showed one or two points of interest. The patient was brought to the hospital for nothing definite. He was a rachitic child with a large spleen and also some enlargement of the liver. The blood count showed 1,200,000 red cells and barely more than 8,000 white cells. The diagnosis lay between a splenic anemia, a leukemia or a pseudo-leukemic anemia of the von Jaksch type.

CARCINOMA OF THYROID IN A BOY AGED TWELVE. E. G. SLESINGER, Proc. Roy. Soc. Med. **20**:192, 1927.

Dr. Slesinger reported a case of carcinoma of the thyroid in boy, aged 12. The family history was negative. The patient had been deaf and dumb all his life, and had had a swelling of the neck since birth. At 10 years of age, this swelling commenced to grow rapidly. At first it was smooth and uniform, but later it became irregular and nodular. The boy suffered from stridor on exertion. No glands were palpable, and the spleen was normal. Roentgenograms of the chest showed large root shadows and increased striation spreading to the right apex. A full blood count was given in a report. A portion of thyroid was removed, and Dr. G Nicholson reported the condition to be basal cell carcinoma of the thyroid.

CHRONIC RENAL DISEASE WITH BONY CHANGES. A. A. OSMAN, Proc. Roy. Soc. Med. (Clinical Section) **20**:1041 (May) 1927.

The case reported occurred in a boy, aged 12. In addition to chronic nephritis, the patient showed bony deformities. At the age of 5 or 6, he complained of weakness in his legs. On admission to the outpatient department, on Aug. 25, 1926, he was pale, thin and undersized, with a marked genu valgum. The roentgenographic appearances of the bones were not typical of renal dwarfism or late rickets. The urinalysis, the blood count and the report of the roentgenogram of the kidneys are given in the report. The case was shown in order to elicit opinions as to a possible connection, if any, between the bony and renal lesions.

WILLIAMSON, New Orleans.

VACCINE THERAPY IN INFANTILE ASTHMA. MINET and POREZ, Arch. de méd. d. enf. **30**:399, 1927.

Although a specific has not yet been found for asthma, either in early or in adult life, recent investigations in the pathogenesis of this disease have enriched the knowledge tremendously and have practically divided its study into two distinct fields. One of these concerns itself with the part possibly played by a disequilibrium of the vegetative nervous system, particularly in hypervagotonia, and the other, with a humoral imbalance or humoral shock provoked by a multitude of agents acting as true sensitizing antigens. The treatment for asthma has been profoundly affected by these new conceptions; for example, certain forms are now being relieved by the process of desensitization. Following Nobecourt, the authors classify infantile asthma into three groups: (1) asthma associated with alimentary anaphylaxis, (2) essential asthma and (3) asthma complicating diseases of the respiratory tract. They believe that in the two latter groups, which include the majority of cases, vaccine therapy is the best treatment. Minet's formula, comprising the usual bacteria found in the sputum of these patients, plus *Bacterium pyocyaneus*, is

employed, and two series of ten injections each are made. The inoculations are given every other day for the first five doses, with a delay of five or six days between the fifth and sixth injections.

The favorable action noted in numerous cases reported is believed to be due to an actual bacterial desensitization following some acute infection in the upper respiratory passages.

LYMPHATIC COLITIS, THE MOST COMMON SYMPTOM OF LYMPHATISM. SITTLER, Arch. de méd. d. enf. **30**:455, 1927.

The author believes that the syndrome constituting lymphatism and the picture commonly interpreted as arthritism are frequently confused. Children of arthritic stock often show lymphatic hypertrophy and present the clinical aspect of Czerny's exudative diathesis, a term that Sittler feels is misleading, as it ignores the more pronounced lymphatic symptoms.

One of the most common manifestations of lymphatism is an irritation of the descending colon involving the lymphatic tissue; it is due to practically every case to an excess of fat in the diet, whether the patient is a nursling or is in the second year of life. Frequent stools, composed largely of mucus and occasionally tinged with blood, accompany this condition; complicating it, there is often a severe congestion of the liver, with involvement of the adenoid tissue of the upper respiratory tract.

Sittler believes that the abdominal pains, particularly about the navel, in this type, are due to irritation of the lymph nodes entirely. The syndrome is promptly relieved by withholding fats.

AMESSE, Denver.

A CONTRIBUTION TO THE STUDY OF CHRONIC PURPURA WITH THROMBOPENIA. H. H. LAUTIER, C. OBERLING and P. WORINGER, Rev. franç. de Pédiat. **3**:341, 1927.

The authors report a case of purpura with repeated epistaxis occurring in a child, aged 5. Purpuric spots had appeared for the first time at 2 years of age. On admission to the hospital the hemoglobin was 10 per cent and the platelets 10,000; the coagulation time was normal, but the bleeding time much prolonged. The child was weak, and the general condition and blood picture improved only temporarily after repeated transfusions. Splenectomy was resorted to and was followed by cessation of the epistaxis and marked increase in the platelets. However, the child died five days after the operation with a bronchopneumonia.

In a study of the autopsy material, great interest attaches to the bone marrow. This was hyperactive, as would be expected, but the examiners were struck by the marked diminution in the megacaryocytes and the pathologic condition of those present. The nuclei showed pyknosis and karyorrhexis and the cytoplasm large granulations with many vacuoles. The authors feel that the diminution in platelets may be directly related to the abnormalities of the megacaryocytes.

LESLIE, Chicago.

FOREIGN BODIES IN THE BRONCHI. C. ANTONIO, Clin. pediat. **9**:172, 1927.

When a child formerly in good health is suddenly seized with symptoms of suffocation, cyanosis and asphyxia, with later signs of localization in the respiratory system unilaterally, a foreign body should be suspected. Following the acute attack, there may be asthmatic breathing and pertussoid cough. The physical signs on the affected side are diminished vocal fremitus and decreased

intensity of the respiratory murmur. A negative roentgenogram does not exclude the presence of a foreign body. The treatment is expectant, and emergency tracheotomy should be done when indicated. The right bronchus is the most frequent localization. A case is reported in which a foreign body became lodged in the left bronchus. It was discharged spontaneously, and an uneventful recovery followed.

NONSPECIFIC PROTEIN THERAPY IN BRONCHOPNEUMONIA. G. HALFER, Clin. pediat. **9**:237, 1927.

The author used nonspecific protein therapy in twenty-four cases of grippal bronchopneumonia, with recovery in each case. In six cases of postpertussis bronchopneumonia, recovery occurred in four and death in two cases. Ten patients having bronchopneumonia following measles were treated, with complete recovery in all.

PRIMARY LYMPHOSARCOMA OF THE THYMUS. ELISA ZANELLI, Clin. pediat. **9**:241, 1927.

A child, aged 10, presented a symptomatology characteristic of mediastinal compression — cyanosis, stridulous respiration, sibilant inspiratory murmur, spasmodic dry cough, dyspnea, anisocoria and voice changes. Pleural effusion was also present. The patient died suddenly of asphyxia.

At autopsy, a tumor mass was found in the upper part of the chest anteriorly, invading the anterior and posterior mediastinum. The right lung was pushed over to the right side. The trachea, esophagus, ascending aorta, aortic arch and superior vena cava were entangled within the neoplasm. Metastatic nodules were found in the right lung and pericardium. The peribronchial lymph glands were small and did not present any changes due to the tumor. Histologic examination revealed a lobulated lymphosarcoma of the thymus. The author considers it as primary in the thymus.

ETIOLOGY AND PATHOGENESIS OF SECONDARY PURPURA. A. SIRCA, Clin. pediat. **9**:467, 1927.

Infective and toxic factors undoubtedly play an important part in the etiology and pathogenesis of secondary purpura in infancy, but only when conditions essential for its manifestations are previously present in the organism. This so-called preparatory stage in the evolution of the disease is important. Preexisting changes may be found in the hemopoietic, reticulo-endothelial and endocrine systems.

Two cases are reported. In one case the purpura was secondary to a protracted malaria, and in the second case it occurred as a complication of septicemia following a pneumococcus pleurisy.

ZAMBARANO, Northville, Mich.

THE SECRETORY FUNCTION OF THE STOMACH IN THE NURSING CHILD. DINO MOGGI, Riv. di clin. pediat. **25**:361, 1927.

The author examined the stomach contents of thirty children of from 1 to 17 months of age; twenty-four did not show any gastric disturbance, and six showed vomiting or dyspepsia. In two cases of pylorospasm, there was hyperacidity and in one of vomiting from overfeeding, hypo-acidity. In two cases of simple dyspepsia and five atrophic infants, the gastric contents were normal.

CONGENITAL LYMPHOSARCOMA OF THE LIVER. VITTORE ZAMORANI, Riv. di clin. Pediat. **25**:456, 1927.

A case report is given of an infant born with a large liver and subcutaneous tumors. Death occurred when the child was 31 days old, and necropsy established a diagnosis of congenital lymphosarcoma of the liver with metastases.

HIGGINS, Cincinnati.

SYNTHALIN THERAPY AND ITS ACTION. POUL IVERSON and J. MUNCK, Ugesk. f. Læger **89**:533, 1927.

Five patients suffering from diabetes mellitus were treated with synthalin. The effect of injections of synthalin into normal individuals is also shown. Synthalin does not consistently lower the blood sugar in the sick nor in the well individual.

The conclusions of the authors' own observations are as follows: 1. The drug has a toxic action, if given in a moderately large dose, and causes such symptoms as dyspnea, anorexia, diarrhea, apathy and headache. 2. It influences, somewhat, the carbohydrate metabolism in the same way that insulin does, though it is not so prompt nor effective in acidosis. 3. It appears to have a certain therapy, but it is of limited value and should be tried when insulin is not effective.

PRELIMINARY OBSERVATIONS IN THE SYNTHALIN TREATMENT OF DIABETES MELLITUS. J. E. HOLST, Ugesk. f. Læger. **89**:540, 1927.

Ten patients were placed on synthalin therapy. Five showed definite improvement and five not any improvement.

The tolerance for synthalin is markedly variable in different individuals, and consequently a definite schematic system of dosage cannot be worked out. The best results with synthalin are obtained in cases in which small amounts of insulin are needed, and the insulin is kept up until the cumulative effect of synthalin is apparent.

SCHULTZ, Minneapolis.

CHYLANGIOMA AND CHYLE FISTULAS OF THE LOWER EXTREMITIES AND OF THE EXTERNAL SEX ORGANS. C. KNAPPER, Nederl. Tijdschr. v. Geneesk. **71**:2089, 1927.

This article contains an extensive description of a case in which the chyle, which normally is found only in the chyle ducts of the mesentery, penetrated into the lymph vessels of the leg up to the popliteal space by way of the cisterna chyli. This rare condition was found in a boy, aged 5; infection with *Filaria nocturna* (Bancrofti) could be excluded. The first symptoms were noted at the age of 3 weeks, when the mother of the child found that the right leg suddenly swelled, the swelling gradually extending over the exterior sex organs. Once, when the child was 4 months old, a flow of chyle occurred from the penis. At the age of 1 year, circumcision had to be done; until the age of 4 years, there were no special complaints. The boy then suddenly had severe pain in the right leg, with high fever. After operation, which showed a diffuse extension of the lymph system in the subcutaneous tissue of the right leg with a chylous content, the boy was free from symptoms for one year. A swelling then developed in the right fossa poplitea, and a radical operation was performed.

Only twelve other cases of this rare condition were found in literature. The disease is called chylangioma diffusa of the truncus lumbalus. The lymph

ducts of the truncus lumbalus are dilated; they have either an insufficient valvular system or none, and this causes the chyle to penetrate into the pathologically changed region of the lymph ducts. It can be said with certainty that the condition is not the result of an insufficient discharge by way of the ductus thoracicus. Clinically, the condition is characterized by a slowly increasing swelling of the legs and of the exterior sex organs (elephanthiasis). Afterward yellow-white vesicles appear on the skin; these vesicles rupture and discharge chyle. Finally, a chylous fistula is developed, which may be dangerous because of infection and the exhaustion resulting from the loss of chyle. The development of these fistulas may be prevented by breaking the direct communication between the ductus thoracicus and the peripheral lymph ducts. For such an operation a laporotomy is necessary, as was done in the case described. The result of the operation was determined by adding to the patient's food a fat having a specific reaction. On puncture of the popliteal space, no evidence of this fat was obtained.

It may be said with certainty that the same disease is also known in the region of the truncus cervicalis and probably also in the region of the truncus subclavicus, as well as in the other supplying lymph ducts of the ductus thoracicus.

VAN CREVELD, Amsterdam.

Nervous Diseases

KETOGENIC DIET IN TREATMENT OF EPILEPSY. W. A. SMITH, Piedmont Hosp. Bull. **4**:6 (March and April) 1927.

The author, using the usual ketogenic diet in children, supplies vitamins — the water-soluble in 5 and 10 per cent vegetables; the fat-soluble in butter, cream and eggs. Saccharine is allowed for sweetening. He finds that the principal difficulty is the tendency of the children to eat candy. It is useless to attempt a dieting treatment if they persist in this tendency.

SANFORD, Chicago.

A CASE OF MONGOLIAN IDIOCY OCCURRING IN ONE OF MALE TWINS. GORDON CHOWN, Canad. M. A. J. **17**:943 (Aug.) 1927.

The author presents a case of mongolism in one of male twins. The mongolian twin was born two days after the normal infant; the delivery was instrumental.

MOORE, Omaha.

HEMIPLEGIA ASSOCIATED WITH EXTENSIVE NAEVUS AND MENTAL DEFECT. T. BRUSHFIELD and W. WYATT, Brit. J. Child. Dis. **24**:98 (April-June) 1927.

Three cases are described by the authors. The clinical and pathologic symptoms of case 3 are to be reported later. The clinical features that these cases show are the following: (*a*) mental defect, low grade imbecility; (*b*) hemiplegia, left in two cases, right in one; (*c*) nevus, covering about one third of the skin, more extensive on the sound arm and on the paralyzed leg.

LANGMANN, New York.

CASE OF HYPERKINESIS OF DOUBTFUL CAUSE. DOUGLAS FIRTH, Proc. Roy. Soc. Med. **20**:46 (July) 1927.

A girl, aged 2 years, had been normal until March, 1927, when she lost the use of the limbs and kept moving the hands aimlessly. On admission to the hospital, there were incessant movements of the hands, in which both choreiform and athetoid elements were present. She could not feed herself. There was no pyramidal lesion.

SPASTIC DIPLEGIA. NEIL HOBHOUSE, Proc. Roy. Soc. Med. **20**:49 (July) 1927.

A girl, aged 4½ years, was admitted to the hospital in February, 1927, with moderate spastic weakness of the right arm. Supination was limited. There was considerable spasm of the legs. The sound arm was bandaged to the trunk, and active movement in the spastic arm was rapidly increased. The child was taught to walk in a wheel-supporting frame, and after a week or so could push a doll's perambulator. However, she was not able to get the right heel to the ground owing to active spasm of the calf. On April 8, the nerve to the soleus was exposed and injected with absolute alcohol. It was hoped that the child could walk alone by the time that power returned to the soleus, function being maintained in the gastrocnemius.

TUBERCULOMA OF CEREBELLUM. STANLEY WYARD, Proc. Roy Soc. Med. **20**:52 (July) 1927.

The patient had suffered from enlarged cervical glands since June, 1924. On March 4, 1927, they were dissected. On March 5, the temperature was 102 degrees, and the patient complained of headache. On March 11, the mental state was dull. The rigidity of the neck and the Kernig's sign were marked. The cerebrospinal fluid showed a marked lymphocytosis. There was no change in the ocular fundi at any time. On March 25, the mental condition was improved, and from that date the patient made a steady progress toward recovery.

WILLIAMSON, New Orleans.

TETANY DIATHESIS AND HYPOCALCEMIA. L. D. VERONESE, Clin. Pediat. **9**:165, 1927.

Tetany is a form of constitutional diathesis, present in the individual throughout life, similar to other diathetic states such as the lymphatic, uremic, neuroarthritic, hemophiliac, hypothyroid, hypogenital, etc. Many of the accepted pathogenetic factors (avitaminosis, intoxication) are merely accessory and exciting causes. Tetany is primarily due to imperfect parathyroid function, and by hormonic influence other glands of internal secretion become involved, especially the thymus, in the early months of life. Some patients present symptoms of a latent tetany and only show the characteristic signs and symptoms when hypocalcemia occurs. Infants having tetany fall into the so-called group of "nervous individuals" in later life.

ZAMBARANO, Northville, Mich.

CEREBROSPINAL MENINGITIS FROM PFEIFFER'S BACILLUS IN CHILDREN. BRUNO TRAMBUSTI, Riv. di clin. pediat. **25**:471, 1927.

There have been 569 cases of meningitis in the pediatric clinic at Florence from 1892 to 1926.

Causing Agent	Number	Per Cent	Per Cent Cure or Improvement
Tubercle bacilli	339	59.6	.3
Meningococci	167	29.4	49.1
Pneumococci	29	5.1	0
Influenza bacilli	27	4.7	0
Streptococci	5	.9	0
Staphylococci	2	.4	0
	569	100.1	

The author has made a study of influenzal meningitis, making use of the 27 cases in his own clinic and 217 cases gathered from the literature. When the age was ascertained, 81.7 per cent of the patients were under 2 years and 18.3 per cent over 2 years of age; 26.5 per cent of the patients over 2 years of age and 2.7 per cent of those under 2 years were cured.

HIGGINS, Cincinnati.

Miscellaneous

STATISTICAL REPORT OF INFANT MORTALITY FOR 1926 IN 675 CITIES OF THE UNITED STATES. American Child Health Association, June, 1927.

This report may be summarized as follows:

1. Infant mortality rates are presented for 613 of the cities in the United States birth and death registration areas, and sixty-two of the cities in the death registration area only.

2. Four hundred and eighty-five (79 per cent) of the 613 cities of the birth and death registration areas reporting, and thirty-four (55 per cent) of the sixty-two cities of the death registration area reporting, have infant mortality rates between 50 and 99.

3. The infant mortality rate for 1926 in 613 of the 644 cities of the birth registration area is 73.7. This represents an increase instead of a reduction over 1925, when the rate for 632 cities was 72.6. The lowest rate so far attained was 72.2 for 629 cities in 1924.

4. The median infant mortality rate for the urban population of states of the birth registration area reporting was 77. The lowest urban rate for states of the birth registration area reporting was 39, the highest, 111.

5. Among the largest cities, those over 250,000 population, Portland, Ore., had the lowest rate, 39. Seattle was second with a rate of 47 and San Francisco third with 50. It is of interest to note that the states in which these cities are located rank in the same order when the rates of all of their cities reporting are considered.

6. The three lowest cities in the population group from 100,000 to 250,000 (1920 census) were New Haven, Conn., 54, St. Paul, Minn., and Cambridge, Mass., each with 56.

7. Low rates among smaller cities were those reported from Oak Park, Ill., 35, Pasadena and Berkeley, Calif., 36. and 37, respectively, and Everett, Mass., 39.

8. The rate for New York and Chicago (the two largest cities) was 67 in each, which represents a rate of nearly seven points below the average for the entire country.

LESLIE, Chicago.

PREGNANCY FOLLOWING THYROIDECTOMY. A. C. WILLIAMSON, Am. J. Obst. & Gynec. **14**:196, 1927.

Pregnancy following thyroidectomy may be complicated by marked metabolic disturbances and by a high percentage of fetal abnormalities.

In the series of forty-eight patients studied by the author, twenty infants had definite pathologic conditions. No certain type of abnormality seemed to predominate. There were five cases of melena neonatorum; three of enlarged thymuses; four of enlarged thyroids; two of palpable thyroids; two of acephalic monsters; one of cretinism; one of mongolism and two of stillbirth.

The author feels that no patient on whom thyroidectomy has been performed should become pregnant sooner than two years after operation even

though her symptoms are alleviated. In the interests of both mother and infant, frequent determinations of the basal metabolic rates should be made, and the patient should be treated cautiously with iodine, thyroid substance, sedatives and rest.

ALLEN, Chicago.

THE IMPORTANCE OF TRANSFERENCE IN CHILD HYGIENE. JOHN HOLLAND CASSITY, M. J. & Record **125**:611 (May 24) 1927.

In many child hygiene clinics over the country, the efforts of the physicians are devoted exclusively to the correction of faulty environmental situations which contributed to the child's maladjustment. The psychoanalytic approach should receive more attention. The child may not understand the nature of his repressions, but it is through the transference that he improves or recovers. What happens with a good transfer is that affective autonomic tensions are released through verbal discharge. The child feels relieved when he takes the physician into his confidence and tells him all his troubles. In the process, the patient is enabled to release energy that has been pent up and spuriously fixated on some object of love or hate.

Several cases are cited in which children showing maladaptations have been improved or cured by effecting a transference.

CHEST EXAMINATION IN INFANTS AND CHILDREN. JOSEPH H. MARCUS, M. J. & Record **125**:618 (May 4) 1927.

Finger percussion should be the only form used in this examination. Light percussion should usually be used, but in determining solid areas deep within the chest heavy percussion should be used.

The easiest way to examine the front of the chest is when the infant is lying in some one's lap. When the back of the chest is examined the infant should be held in some one's arms with its arm around the neck. It is wiser to use auscultation before percussion, because it frightens the child less. The percussion note is more resonant during childhood than later. D'Espine's sign should be looked for while examining the chest. The sense of resistance felt by the finger often gives more information than the sounds elicited by percussion.

The puerile type of respiration in children is often mistaken for bronchial breathing. Sounds similar to râles may be made in the nose and pharynx. These sounds in young children may be transmitted downward and heard over the lungs. If they are made in the upper air passages, they are heard over both lungs and are the same over both sides. They can also be heard over the neck and sometimes over the cheeks. Râles made in the bronchi are not heard in these situations and are never exactly the same on the two sides.

WILLIAMSON, New Orleans.

COMMONLY CONFUSED DISABILITIES OF THE HIP JOINT IN CHILDREN. RICHARD B. DILLEHUNT, Northwest Med. **26**:254, 1927.

There is a tendency to make a diagnosis of tuberculosis in every form of painful hip with restricted motion. Fortunately most pathologic hip joints in children are not tuberculous. Of ninety-four patients with disease of the hip from the Shriners' Hospital for Crippled Children twenty were tuberculous; fourteen had Legge's disease; six, coxa vara; twenty-eight, congenital dislocation; fourteen, osteomyelitis or septic arthritis, and six had arthritis of unknown cause. The remaining six had uncommon disorders. The symptoms and differentiation of each condition are outlined. The author calls attention to four important and

valuable points. (1) If a joint cannot be moved in any direction without severe pain, there is a generalized pathologic condition within the joint. (2) If movable in one or more directions without pain, the disease is near to but without the joint. (3) When osteomyelitis occurs in a bone near a joint, an effusion containing leukocytes, resembling pus, is formed, but it is sterile. (4) Aspiration under aseptic conditions is always safe. If the fluid is clear or blood-tinged and contains streptococci the joint should be immobilized, but not drained. If it is frankly purulent and shows staphylococci, it should always be drained widely. A joint with sterile fluid should never be drained. In all disorders of the hip, treatment must be directed to prevent the all too frequent deformity.

SCOTT, Philadelphia.

NATURAL IMMUNITY TO INFECTION AS OBSERVED IN NATIVES OF THE TROPICS. R. W. MENDELSON, South. M. J. **20**:501, 1927.

Statistics are presented to show that natural immunity to infection is developed by persons living in a highly infected environment under natural conditions.

The author concludes that clinical experience in the tropics leads one to believe that the new-born infant does inherit sufficient immunity to general infection to protect him until more specific immunity is developed. One exception to this general statement is encountered in tetanus. This disease is fatal to infants.

SCHLUTZ, Minneapolis.

ANALYSIS OF ONE HUNDRED CASES OF FITS. S. H. COOKSON, Arch. Dis. Childhood **2**:178 (June) 1927.

The patients varied in age from 6 weeks to 11½ years. Most of them were less than 1 year old at the time of onset; fifty-five were boys. There was a family history of epilepsy in 20 per cent. Petit mal was as prevalent as grand mal; only two cases had aurae, but many of the patients were rather young. Lumbar puncture in six cases revealed no abnormality. Bromids and phenobarbital were used for treatment. Petit mal did not respond to the treatment.

PETERMAN, Milwaukee.

RETARDED RATHER THAN ARRESTED DEVELOPMENT. OMBREDANNE, Arch. de méd. d. enf. **30**:339, 1927.

Strictly speaking, an arrest implies a definite suspension in evolution. Ombredanne, pediatric surgeon at the Hospital for Sick Children, Paris, contends that certain conditions usually described as due to arrested development are often states of retarded evolution instead, which may progress to completely normal conditions after birth.

He cites the fontanel as an instance of this physiologic slowing up of embryologic processes. In abdominal operations clinicians have frequently noted the entire absence of the coalescence commonly found in adults between the ascending colon and the posterior parietal peritoneum. It may be concluded that this particular phase of evolution is usually not completed until postnatal life. This is also true of congenital inguinal hernia. In certain types of spina bifida, while the tumor itself is not absorbed and consequently never disappears spontaneously, certain evolutionary changes occur in its primitive coverings during the first few years of extra-uterine life, which transform this elementary integument into normal skin and enable the surgeon to operate successfully.

AMESSE.

EXPERIMENTAL STUDIES ON THALLIUM ACETATE. E. FANTON, Clin. pediat. **9**:83 (June) 1927.

Thallium salts were used for a long time in the treatment of night sweats in tuberculosis. They were also used in typhoid fever, blenorrhagia, cancer and malaria. In dermatology, thallium was considered a drug of great value. It fell into disuse because of the difficulties encountered in obtaining pure preparations. The author has made an extensive study of the effects of the acetate of thallium in rabbits.

In rabbits, the dose of the drug should not exceed 5 or 6 mg. per kilogram of body weight. The earliest toxic manifestations following an overdose are: falling out of the hair and the formation of zones of alopecia in scattered parts of the body. The blood shows increased coagulability, increased viscosity and increased hemoglobin content. The red cells are increased or slightly diminished in number and some of them show granular degeneration. The polymorphonuclear neutrophils are diminished; eosinophlic myelocytes are present; the eosinophilic polymorphonuclears are slightly increased; lymphocytes are markedly increased. Loss in weight is slow and usually begins when digestive symptoms become marked. In acute intoxication by the drug, the temperature of the body drops; in chronic poisoning, it remains unchanged. From four to seven weeks after intoxication, opacity of the crystalline lens is observed. Total bilateral cataract also was seen. In the urine there were many bile pigments, albumin and an abundance of phosphates. At autopsy, lesions of the liver, spleen and kidneys were found. Rachitiform changes were observed in the long bones.

ZAMBARANO, Northville, Mich.

DIRECT MEASUREMENTS OF THE BODY SURFACE OF CHILDREN. G. FRONTALI, Riv. di clin. pediat. **25**:241, 1927.

The author used the Bordier integrator (J. de physiol. et de path. gén., September, 1901) to determine directly the body surface of 33 children ranging from 24 days to 12 years of age. The results are compared with those obtained for the same children by calculation from the formulas of Vierordt-Meeh, of Lissauer and of DuBois. The formula of Vierordt-Meeh gave results from 9 to 29 per cent higher than those obtained by the direct method. Only two of the thirty-three calculations by Lissauer's formula varied by 10 per cent from the direct measurement, eighteen being higher and fifteen lower than the direct method. The calculations by DuBois' method were less than by the direct measurement in all but seven of the thirty-three cases; in eleven of the thirty-three cases, the difference was more than 10 per cent.

AN ASPIRATION APPARATUS WITH VARIOUS USES. BRUNO TRAMBUSTI, Riv. di clin. pediat. **25**:256, 1927.

The author describes a specially blown glass tube for use in various clinical and laboratory procedures when aspiration under sterile precautions is desired, as in drawing blood for transfusion.

THE OCCURRENCE TOGETHER OF SOME CONGENITAL MALFORMATIONS: CARDIAC DEFECT AND FUNNEL-CHEST. DOMENICO LARINI, Riv. di clin. pediat. **25**:384, 1927.

Congenital malformations of the chest are often associated with congenital malformation of the heart. The author believes that a single alteration of development in the embryo is responsible for this concomitance.

HIGGINS, Cincinnati.

FETAL RHABDOMYOMA. GUSTAV PROCHAZKA, Čas. lék. česk. **64**:1476 (Oct.) 1925.

The author describes in detail a multiple rhabdomyoma musculorum cervicis in a cow's fetus of six months. The histologic study shows that this was a rhabdomyoma and not a rhabdomyoma sarcomatodes, which is more common.

STULIK, Chicago.

A DISEASE PECULIAR TO JAPANESE CHILDREN AT THE TIME OF DENTITION CAUSED BY LEAD-POISONING FROM THE FACE POWDER USED BY THE MOTHERS. I. HIRAI, Bull. Oriental Child. Health A., Infant Series **1**:1 (Feb.) 1927.

This disease is one of the chief causes of infant mortality in Japan and has been prevalent for the last 200 years. The clinical symptoms are vomiting, bloody diarrhea, convulsions and jaundice. The usual age of onset is 8 months, and the disease is more prevalent in hot weather, due to the increased use of face powder. Death usually results, and considerable lead is found in the body postmortem. The source is always traceable to the white powder used by the mother.

H. N. SANFORD.

Society Transactions

ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

Washington, D. C., May 17, 1927

F. P. Gengenbach, M.D., *President, in the Chair*

Dietetics in Pediatric Teaching. Dr. F. P. Gengenbach.

Since the ingestion of food is necessary for the maintaining of the continuity of life and a proper balancing of that food for the successful growth of the infant, dietetics should be one of the most important subjects dealt with in pediatric teaching. While emphasis has been laid on the subject of infant feeding for many years, little time is ordinarily spent on the later feeding of children, especially after the second year.

Owing to the rapid advances constantly made in the prevention of disease, the physician must more and more assume the rôle of adviser and teacher of his patients in proper methods of living. Of these methods, the subject of dietetics is certainly one of the most important. Students should therefore be taught both the art as well as the science of proper preparation and balancing of foods and the inculcation of proper feeding habits for the growing child through the medium of its parents.

Nature vs. Science. Dr. M. L. Turner.

Students are taught to feed infants and children incorrectly, as may be seen by observing the way young animals are fed. All animals begin to nurse a few minutes after birth, and under these circumstances they do not take water during the first few weeks of life. Moreover, they nurse from all of the nipples at one feeding instead of alternating them at different feedings. If an infant gets enough food all of the time he will not overeat and will sleep contentedly, and an infant over 1 year, provided he gets enough food, can be fed successfully on three meals, sometimes two, a day. If older children are given plain food, prepared so that it is not robbed of all its vitamins, three times a day, one will see them eat well and thrive because they are hungry. Concentrated food too often makes for capricious appetites and failure to gain.

DISCUSSION

Dr. John A. Foote, Washington, D. C.: Dr. Turner was not talking about science, as such, at all; he was talking about empiric statements; but is the empiric use of remedies unscientific? I do not think so. Priests and medicine men used them at first in the making of charms and amulets. Some unusually intelligent priest noticed, for instance, that when foxglove was given as a charm to a man who had dropsy, the patient improved. That usually helped him while other things did not help him. After the passage of centuries and countless observation, many things came to be used in this way. This was science, because it was the summation of exact knowledge based on exact knowledge and handed down by tradition.

Old-fashioned people used to give their children bread and molasses. They said it was good for them. It has since been discovered that black molasses contains more iron than any other organic substance. The old southern mammy used to give her children pot liquor; in other words, the water in which cabbage had been boiled. Now it is known that cabbage contains vitamins. This folk knowledge was really scientific knowledge.

DR. JOSEPH BRENNEMANN, Chicago: I think that Dr. Turner's paper contained good "horse sense"; I think this is due chiefly to the fact that he evidently has gone deeply into veterinary science. That brings up this point: I have an idea that one would know more about pediatrics if one knew what the veterinarians do. They know more about some things of that sort than pediatricians do, and a good deal of advancement in pediatrics resulted from experience connected with that sort of work. I have always had a feeling that some time I should like to get a fairly good knowledge of veterinary science. It would be excellent if, in connection with the medical school, there were a course in comparative infant feeding — what is done with calves, pigs and colts.

One of the most valuable books that I have in my library is Brüning and Schwalbe's "Allgemeine Pathologie." This book treats of the comparative pathology of animals and man.

THE TEACHING OF PEDIATRICS: A PLEA FOR SOME CHANGED CONCEPTS. DR. JESSE R. GERSTLEY.

First, what is pediatrics? It originated from internal medicine as a specialty, but in its growth it has fused again with the mother subject. Pediatrics is greater than a specialty. It is the subject of internal medicine applied to children. Specialties, in a way, limit themselves to the study of the effects of disease on an organ or a group of organs. The specialties originate from the failures of internal medicine and pediatrics. But the contributions of the specialists, being limited by the very scope of their work, are largely matters of technic or bits of special knowledge. Operations have been performed in cases of otitis media and mastoid disease for years and will continue to be, but it takes a Dick or a Tunnicliff to cure and to prevent the dread diseases from which these complications spring. Pediatrics, then, ranks with internal medicine as a basic study. It deals with the patient as a whole. It is internal medicine and is not a "specialty."

For some obscure reason, deans of medical schools have never sufficiently emphasized the importance of pediatrics. While pediatrics shares all the problems of internal medicine, its contributions have been greater than those of the mother subject. The great reduction in mortality in recent years has been due largely to the efforts of the pediatricians. The introduction of the great subject of nutrition comes from the same source, and certainly pediatricians may lay just claim to being pioneers in the practice of preventive medicine.

What are the boundaries of pediatrics? If pediatricians unite in attempting to gain more recognition for their subject, they themselves must be agreed as to its boundaries. I believe that all pediatricians are unanimous in including preventive work for both nutrition and infection. Should they delve into the newer problems, those of environment and behavior? I believe that they should. They must grasp any problem within their field, and that field is "the child as a whole."

Of the defects in the present system of teaching pediatrics, overscientific training is certainly not one. In spite of the multitude of protests against the apparently excessive amounts of science taught in our institutions, I feel that in the broad sense of the word, the curriculum is not sufficiently scientific. Lack of science is manifested in two ways. The first is the lack of correlation between the various subjects in the school. Instead of the laboratory and the clinical units as well as the various specialties being fused to further one great purpose — the benefit of the patient as a whole — each exists independently. Each is an end in itself rather than a means to an end.

The second way in which science is lacking in the teaching of the medical school is the absence of any concerted attempt on the part of the teachers to influence the mind of the student. Students are taught knowledge but are not taught to think scientifically. Students are not taught to discriminate between true and false conclusions.

To correct these defects, a reorganization of the medical schedule would be necessary. For a certain period each day, the students should attend a clinic, during which a representative of every laboratory and clinical subject concerned with that particular patient would participate in the discussion. The students must learn that all their courses are related to their future patients.

To instil a scientific attitude in the mind of the student could not be a part of the medical curriculum. This becomes a duty of the individual teacher. Science is not a thing to be taught; it is a state of mind. The teacher has no better method than setting a good example. He should be actively engaged in some research. By sharing his problems with his students, he can give them some insight into scientific thinking.

Other phases of pediatrics that are neglected are therapeutics, dentistry, diagnostic treatments, infant welfare, medical asepsis, contagious disease and the new subject of behavior problems.

DISCUSSION

Dr. S. W. Kelley, Cleveland: All that I could add to Dr. Gerstley's description of the range of pediatrics is that pediatrics should include not only the medical side but the surgical side of the work.

The Technic of Teaching. Dr. John Lovett Morse. (Published in full in this issue.)

The Correlation of Preventive Pediatrics with Clinical Teaching. Dr. W. L. Funkhouser.

Preventive medicine has supplied and will continue to supply the opportunity for speculative medicine. In consequence of research in this field, morbidity and mortality have been reduced and the life cycle lengthened.

While hygiene and sanitation have been taught for years, only recently has the course of study been lengthened and practical phases so extensively stressed. Even with the thoroughness of present instruction, the average student is unable to evaluate the practical significance unless it is made applicable clinically, just as is done in physiology and pathology.

Those who teach pediatrics appreciate the applicability of preventive medicine to infancy and childhood and even to adolescence. The first effort to invade this field pedagogically was made by the American Pediatric Society's outline sent to teachers of pediatrics. However, this course did not necessarily correlate preventive pediatrics with clinical teachings. The time to teach this phase of medicine is when the opportunity presents itself, especially when demonstrating the end-results of a condition that could have been prevented. While it can be of doubtful value to the case presented, yet it can be made a spectacular example to impress on the mind of the student the opportunity of never letting a patient entrusted to his supervision get into this abnormal state as the result of carelessness, ignorance or neglect. Among these conditions may be mentioned rickets, malnutrition, difficult feeding problems, especially resulting from weaning without cause, congenital syphilis, typhoid, diphtheria, smallpox, faulty posture, faulty habits, and the large group of cases headed toward a neurosis as the result of lack of normal mental hygiene. With so much crowded in the student's curriculum, one should systematize his chaotic mass of knowledge by demonstrating the practicability of his studies, especially as they apply to the clinical branches. For this there is no better opportunity than that afforded by preventive medicine and clinical pediatrics. In the enthusiasm over the existing pathologic condition, laboratory examination or therapeutic regimen, one can so easily overlook the opportunity to demonstrate the practical application of a preventive phase. It is the correlation of preventive pediatrics with the clinical case that will make the greatest impression and thereby give the best result, one that cannot be accom-

plished by a preventive course alone even though it is thorough and comprehensive. If one can instruct the student so as to give him a vision of his opportunity in the application of preventive measures so that he may guide the growing youth away from physical and mental defects, one's efforts will be fully repaid.

DISCUSSION

DR. J. VICTOR GREENEBAUM, Cincinnati: At the University of Cincinnati College of Medicine, we also give a course in preventive pediatrics to the students. We not only do the things that are done in Atlanta, but we send the students into the homes, day nurseries and welfare stations. I think that if medical instructors could teach students to go into the homes and get a complete point of view, they would accomplish what they have set out to do—teaching them to be good physicians.

Book Reviews

THE TEETH AND HEALTH. By J. SIM WALLACE, D.Sc., M.D., L.D.S. Price, $1. Pp. 214. Chicago: Chicago Medical Book Company, 1926.

This little volume is deserving of some credit because of the apparent sincerity of its author. On reading it, however, one is impressed with the fact that it is too complex and involved to be of great value to the lay mind and insufficient technically to be of value to the scientific mind; it falls somewhere midway between the two groups.

The author has a rather strained attitude toward certain types of food and is rather prejudiced with reference to the cause or causes of abrasion. He probably will find few people who will agree that the tooth brush will cause an abrasion.

In his article on pyorrhea he seems to be convinced that it is purely of local origin. On the contrary, it is probably true that pyorrhea is as much a constitutional disease as nephritis. Conditions resembling those in pyorrhea may be brought about by the accumulation of tartar and lack of care. True pyorrhea is seen in mouths in which salivary deposits and pus are not found. He says, "All that need here be said with regard to the peculiarities of the bacteria causing pyorrhea is that they are pus-producing or pyogenic, that more than one species of organism can produce the disease, ..." Against this view are many of the best known investigators, who look on tartar and pus as incidental, and not essential, to pyorrhea.

On the whole, the book has a purposeful outlook, and it is rather unfortunate that it is too complex to be of greatest interest and usefulness to the lay reader.

DIE NEUROSEN DES KINDESALTERS — MIT BESONDERER BERÜCKSICHTIGUNG VON LERNSCHWÄCHE UND SCHWERERZIEHBARKEIT. By W. CIMBAL, M.D., Price, 16.50 marks. 24 illustrations. Berlin: Urban and Schwarzenberg, 1927.

This volume is decidedly more ambitious than most of the books on the mental disorders of children. Furthermore, it is written without any qualification for medical readers. It is refreshing to find a discussion without constant sentimental appeals.

Dr. Cimbal divides and subdivides groups of cases without supporting his classification by clear arguments or by pertinent case histories. In spite of reservations the reviewer believes that this rather formidable volume is valuable and suggestive. It successfully avoids many of the pitfalls into which many propagandists have fallen, by which an argument for a theory is combined with an attempt to describe phenomena.

The author evidently believes that the mental life of children is complicated and worthy of close study by qualified physicians who can decide physical questions as well as mental ones. For such physicians he presents an elaborate classification and describes treatment in which drugs play a surprisingly large part.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION OF DISEASES OF CHILDREN

Chairman: Dr. Hugh McCulloch, 500 S. Kingshighway, St. Louis.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Minneapolis. Time: June 11-15, 1928.

AMERICAN PEDIATRIC SOCIETY

President: Dr. J. Claxton Gittings, 1828 Pine St., Philadelphia.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Washington, D. C. Time: April 30 to May 2, 1928.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Place: Minneapolis. Time: Spring, 1928.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Undecided. Time: May or June, 1928.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto.
Place: Vancouver, B. C. Time: June, 1928.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. O. L. Goehle, 15703 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. H. T. Price, 121 University Place, Pittsburgh.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

President: Dr. Robert A. Strong, Pass Christian, Miss.
Secretary: Dr. Hugh L. Dwyer, Medical Arts Bldg., Kansas City, Mo.
Place: Memphis, Tenn. Time: Nov. 14 to 17, 1927.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 West 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. George E. White, Capitol Theatre Bldg., Windsor, Ontario, Canada.

Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.

Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schultz, University of Minnesota, Minneapolis.

Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.

Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. T. Wistor White, Lister Bldg., St. Louis.

Secretary: Dr. E. H. Rohlfing, 816 Beaumont Medical Bldg., St. Louis.

Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

BROOKLYN PEDIATRIC SOCIETY

President: Dr Harold L. Barnes, 1235 Dean St., Brooklyn.

Secretary: Dr. Charles A. Weymuller, 61 Greene Ave., Brooklyn.

Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.

Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.

Place: Concourse Plaza, 161st St., and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.

Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany, N. Y.

Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. William Ropes May, 8 East 66th St., New York.

Secretary: Dr. Stafford McLean, 17 East 71st St., New York.

Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. Henry J. Gerstenberger, 2103 Adelbert Road, Cleveland.
Secretary: Dr. Charles W. Burhans, 2103 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. F. T. Mitchell, 376 S. Bellevue Ave., Memphis, Tenn.
Secretary: Dr. Arthur G. Quinlan, 1193 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Lucius D. Hill, Medical Arts Bldg., San Antonio.
Secretary and Treasurer: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Place: Houston. Time: December, 1927.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. West, Toronto.
Secretary: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Time: November 17, December 15, February 16 and March 15.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Lawrence T. Royster, University, Va.
Secretary: Dr. William B. McIlwaine, Petersburg, Pa.
Place: Danville, Va. Time: October 17, 1928.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. Roy M. Greenthal, 141 East Wisconsin Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

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